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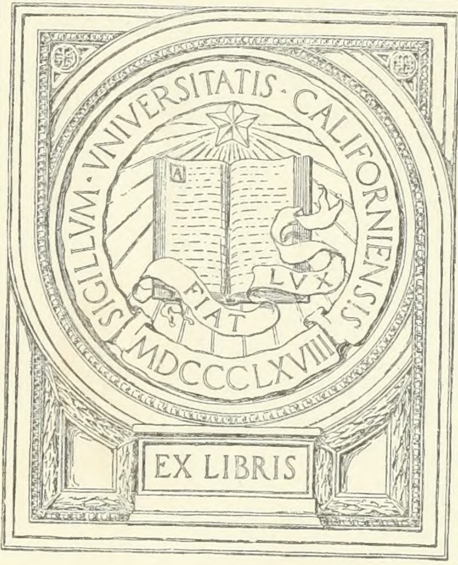

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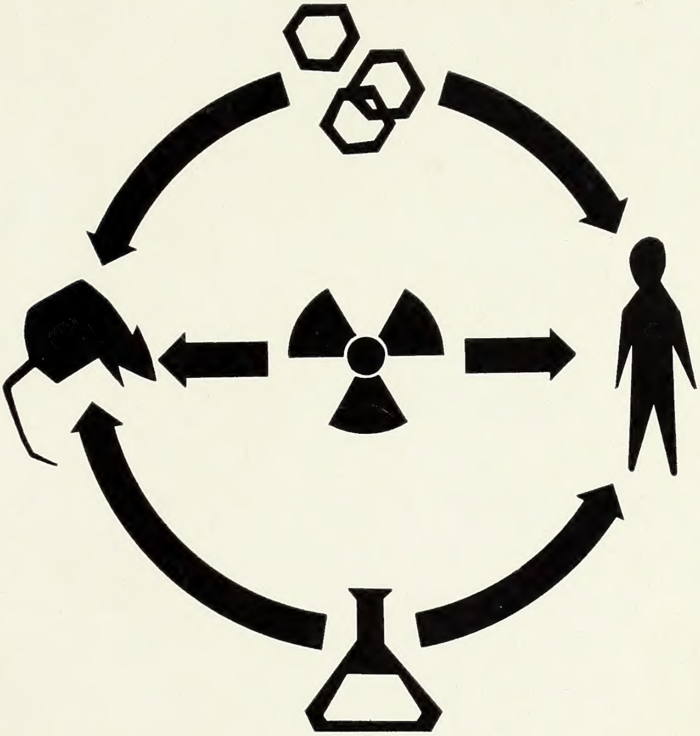
Connecticut Medicine

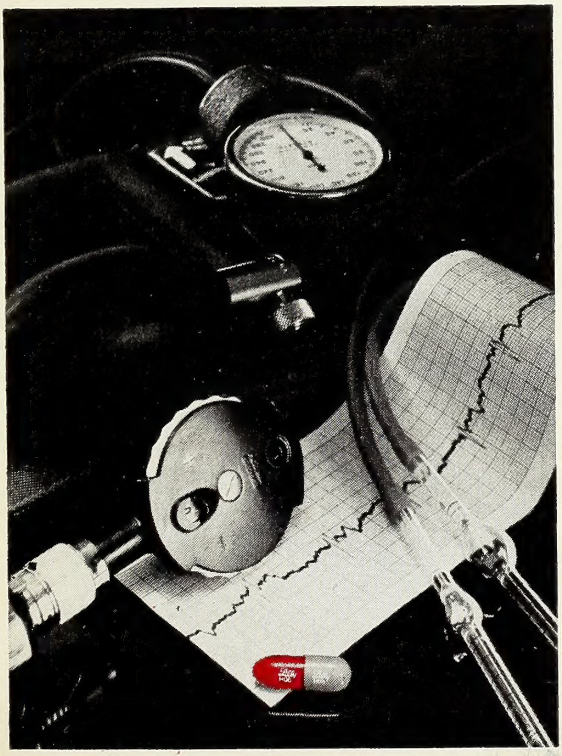
Connecticut State Medical Journal

Volume 32 / January 1968 / Number 1

CLINICAL HEMATOLOGY ISSUE: I. Stuart C. Finch, M.D., *Guest Editor*



The diagram of proven relationships between the development of leukemia in the mouse (left) and virus (top center), radiation exposure (center) and chemical exposure (bottom center). See page 1.



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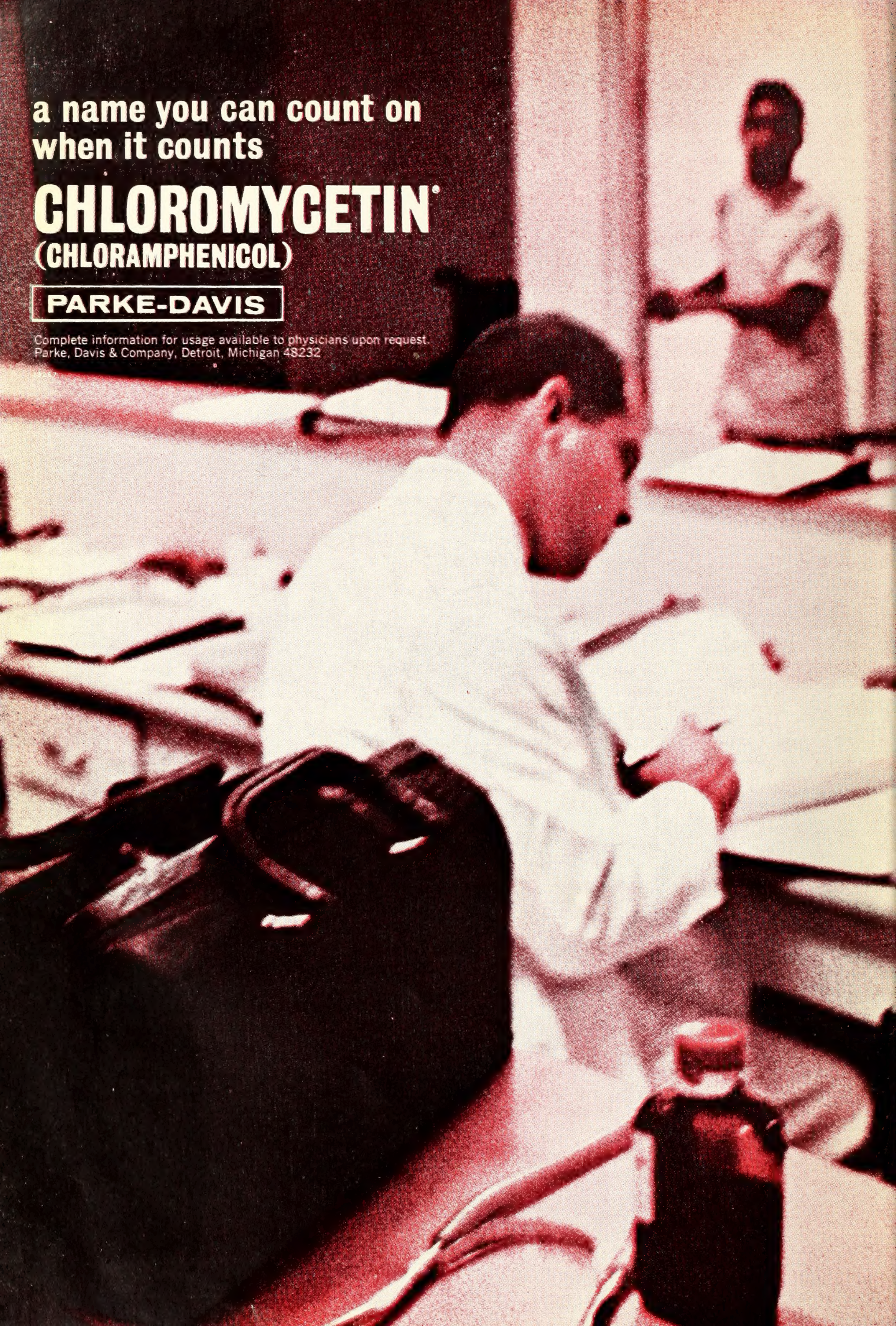
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Connecticut Medicine

JANUARY, 1968
Vol. 32/No. 1

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CONNECTICUT MEDICINE is the official publication of The Connecticut State Medical Society and is published monthly. Administrative Office, 160 St. Ronan Street, New Haven, Connecticut 06511. Telephone 865-0587. Subscription to CONNECTICUT MEDICINE is included in membership fees. Other subscriptions are $10.00 per year; plus $2.00 for additional postage to foreign countries except Canada. Single copies $1.00. Student members, interns and residents may receive Journal subscriptions at half-price, $5.00 per year.

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Connecticut Medicine

editorials

A Look Into The Near Future Of Medicine

This is a revolutionary era. We are in the midst of a great scientific revolution and are experiencing major social and political revolutions. The signs of social and political change are all about us: new nations are struggling for viability, colored people who have suffered deprivation and indignity are demanding political freedom and social justice; undeclared wars are spreading and their effects on the fighting groups threatens to destroy victor and vanquished alike. The population of the world is increasing and taxing our capacity to produce enough food, shelter and education. Urbanization is increasing the problem of housing and transportation. Man is creating serious physical and biological problems by contaminating and polluting the water we drink, the air we breathe and adulterating the food we eat. Our civilization is polluting the air with dinning noises in our environment, producing deafness and anxiety in millions of people.

Man has nevertheless also achieved revolutionary advances in science: progress in nuclear physics, development of atomic energy and exploration of outer space and a remarkable revolution in biomedical science. We have learned more about living matter during the past two decades than in all previous recorded history. We have achieved biosynthesis of nucleic acids and of proteins. Rapidly being clarified are transmission of genetic information from DNA via RNA to protein; the nucleotide code of amino acids is largely established; control of regulatory processes in cellular metabolism is increasingly understood; the role of viruses in the etiology of animal tumors and the mechanism of viral invasion of cells and viral replication are being defined. Powerful electron microscopes have served to develop the science of morphology.

Clinical medicine too has contributed to this mounting tide of discovery. In the last two decades we have witnessed the extraordinary growth of human genetics, the recognition of numerous new diseases, monumental achievements in pharmacotherapy and impressive feats of surgery. These revolutionary changes in science and society pose exciting but also exacting challenges in medical education, in medical science and in medical practice. The physician, if he will but look ahead, has a major opportunity and a major responsibility to help meet these challenges successfully. But to succeed we need to recognize the problems which the physician must face. He must see clearly the consequences of successful cure of infectious diseases; the consequence of rapid growth in population; the changes in political organization and social attitudes which result in the recognition that medical care is a basic human right and that the government is entering this field in a big way to provide for the exercise of this right. He must recognize that progress in science and technology will result

THE COVER

The diagram on the cover of the *Journal* is reproduced from a special virus—leukemia program held in Williamsburg, Virginia, January 9-12, 1967, under the sponsorship of the National Cancer Institute of the National Institutes of Health. The diagram illustrates the proven relationships between the development of leukemia in the mouse (left) and virus (top center), radiation exposure (center) and chemical exposure (bottom center). Both radiation and chemical exposure are of proven importance in the etiology of leukemia in man (right). The viral etiology of human leukemia is uncertain at this time, however, but the relationship is strong enough to justify connecting the symbols for virus particles and man with a reasonably strong arrow.

Editor's Note: Due to a printers' strike there has been an unavoidable delay in the publication and delivery of *Connecticut Medicine*. It is hoped that the February issue will be back on schedule.

in the acceleration of the trend to specialization and subspecialization.

Some of the effects of their developments are readily discernible. There is a growing shortage of physicians and especially the general practitioner. The role of family physician is increasingly assumed by the internist and pediatrician. There is a trend to subspecialization within internal medicine itself which threatens to erode its very concept. The subspecialties are developing the usual organizational patterns of independence and trappings of the parent body: national and international society boards of certification and demands for official recognition and status. These tendencies have profound implications for medical education and medical practice. Already there are special services being established in cardiology, nephrology, hepatology, and hematology. With these developments one can begin to see a withering in the size and value of general services in internal medicine.

The direction of the government's major thrust in health care is now becoming apparent. A recommendation has been made to the president to encourage group practice prepayment plans by amending Title 19 of the SSA to require states to allow medical beneficiaries to use such plans. (1) Their belief is that group practice consisting of family physician, specialists and supporting personnel organized into integrated teams will be able to provide insured families with comprehensive medical services, preventive and therapeutic, of uniformly high quality and at the same time keep the costs down. Increasing subspecialization and increasing diversity and number of paramedical personnel, increasing costs and complexity will doubtless progressively demand a higher degree of organization not present in medical care today.

As the cost of medical care becomes an increasingly important factor in the economy (it is now third but might become the largest industry in this country) cost benefit analysis and more efficient operation will enter seeking to obtain the optimum result for an individual patient at a reasonable cost. The Federal Government has established patterns in dealing with big industries such as utilities which receive direct or indirect government support. Their approach has been not to nationalize but to contract with, support, and regulate these industries. It is a good way of relieving government of the direct burden of producing results. It has also worked out extremely well for the regulated industries by appointing to the administrative agencies, individuals who also have the interest of the industries at heart as well as the public.

Without doubt the efficiency of the individual physician will be improved by three other means. One will be his continuing education in a more aggressive manner. A second will be increasing reliance on existing and new categories of paramedical personnel. A third will be by increasing the use of computers in medicine. One would suppose that it is a waste of scarce health personnel for any to perform tasks below the level for which they have been trained. Federally financed health care programs will probably be used to train physician's assistants, to evaluate their performance and disseminate the results. Mount Sinai Medical School already has such a plan for training such personnel.

Computers will become more and more important in day to day medical care. Properly programmed by the subspecialist and properly questioned by the personal physician they could tremendously expand the scope of the physician. Part of the answer to the problem of continuing education might come from the physician obtaining information from a computer in the diagnosis and management of clinical problems as they arise. However, the physician will also need to devote himself seriously to understanding its theory and practice, its potentialities and limitations. The physician by programming his own history and physical examination for computer recording will become a more skillful clinician and use the computer as an almost limitless extension of his own memory.

New moral and ethical problems are being created by advances in medical science. The difficult problem in donation of organs for transplantation, the choice of patient for chronic dialysis, the moral and biological problems uncovered by the developing science of human genetics. Now that the spontaneous mutation rate is being accelerated by mutagens such as chemicals in our environment and ionizing radiations, we may expect an appreciable and steady increase in the number of newly created genetic disorders. The successes of clinical medicine to heal the sick and prolong life is also aiding in the propagation of deleterious genes which in an earlier era might have been eliminated.

We physicians have a responsibility not only to heal the sick and to prolong life but we have an equal responsibility to do all that is possible to

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render the deleterious genes harmless and to foster favorable progress in mans evolution. This will require voluntary practice of eugenics with active participation of knowledgeable human geneticists in providing counsel and guidance. It will also require active clinical investigation to be concerned with recognition of genetic disorders, with attempts at their amelioration and finally with attempts to minimize their dissemination.

These are only some of the realities of medical care for the near future. The status of the physician in this future depends on how well he can accept and manipulate these realities to the extent of providing the best possible medical care for the public.

L.H.N.

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Urokinase In Acute Pulmonary Thromboembolism

Three types of approaches have been used in an attempt to effect thrombolysis in vivo[1-3]. Among these substances are those whose pharmacologic action results in the release of plasminogen activator such as niacin and independent plasminogen activators such as streptokinase and urokinase. Then there are the combinations of plasminogen activator and plasmin as well as proteolytic enzymes such as aspergillin. Clinical trials of some of these agents have been reported. Thus far no reports on the use of urokinase for the treatment of pulmonary embolism have been reported until the recent paper by Sautter et al[4-6]. Urokinase is isolated from human urine, is a potent plasminogen activator and has been demonstrated capable of producing clot lysis in vitro and in vivo. Theoretically being a human product this enzyme should be much safer than for example streptokinase or lipopolysaccharides of bacterial origin.

Sautter addressed himself to the question as to whether urokinase can reduce the death toll from acute pulmonary embolism since 20 per cent of acute pulmonary thromboembolic disease is fatal. He reports on the use of urokinase in ten patients with acute pulmonary episodes. The clinical diagnosis was confirmed by pulmonary arteriography prior to the institution of therapy. An initial loading dose of 1650 CTA units (Committee on Thrombolytic Agents) per pound of body weight was delivered in a ten minute period. Then equal amounts of the drug were given each two hours for eight hours as a sustained metered infusion. The patients were in the operating room ready for embolectomy had their condition deteriorated. The effect of the enzyme on the fibrinolytic system was followed by measuring the euglobulin clot lysis time every hour. Its effect on mean pulmonary pressure was also measured in each patient.

No complications of any kind were reported during drug infusion, no chill, no major bleeding during or after therapy. Some oozing around the cutdown was observed in all but one patient but not of a troublesome nature. Especially interesting is that post-operative patients did not bleed into the wound. Two patients had received 5000 units of heparin just prior to urokinase treatment and also had no difficulty with bleeding. There was a temporary fall in hemoglobin concentration following urokinase therapy which as yet is unexplained. However, a fibrinolytic effect was obtained in all patients and the prothrombin time which was initially prolonged returned to normal within twenty-four hours. Following treatment there was a fall in pulmonary arterial pressure and in half of the patients this fall, evidencing lysis of the clot in the pulmonary artery, was very dramatic and was paralleled by clinical improvement. The clinical results were judged excellent in eight and good in two patients.

One question that arises is why the variability in response? In evaluating urokinase as a fibrinolytic agent it is quite important to remember that a pulmonary artery embolus is not a fresh clot. It is a clot which has been in the body a varying length of time and during this period has progressed to organization and eventually would become a fibro collagenous scar. It becomes less and less susceptible to fibrinolytic therapy as it contains less and less pure fibrin. It is difficult therefore to estimate the age of the clot before it becomes an embolus, but one can form a rough measure of its maturity by its response to fibrinolytic therapy. The older the embolus, the more difficult it is to lyse. A fibrocollagenous scar would, of course, be completely resistent to any form of fibrinolytic therapy and it is this type of case that theoretically should be subjected to embolectomy.

Sautter points out that in persons over sixty-five years of age the results of pulmonary embolectomy have been quite disappointing. He reports four survivors only out of fourteen such attempts and these were all under age sixty-five. It is for this reason that patients in this age group who were previously considered candidates for pulmonary embolectomy be treated with urokinase even if partial cardiopulmonary bypass is necessary for temporary support. Patients in the younger age groups could be treated with urokinase in the operating suite as they are prepared for pulmonary embolectomy.

Patients with bilateral emboli or with one very large single embolus have previously been considered for inferior vena cava ligation because of the strong probability of death resulting from another embolization. Urokinase availability has altered the authors attitude in such cases away from surgery and in favor of enzyme therapy. In Sautter's series all patients would have been considered for ligation previously, but only two underwent inferior vena cava ligation and these two showed the poorest result in the author's series.

The judgment of severity of case and its response to therapy was made in two ways by amount of obstruction as represented by arteriography and pulmonary artery pressure and clinical response of the patient. Several of the cases who showed little response arteriographically, however, exhibited good clinical response. How to account for this difference between laboratory and clinical judgment? It could be, of course, that lysis in clots in the minute vessels occurs which is not recognized arteriographically and also that there has been some reduction in pulmonary artery spasm.

One difficulty in evaluating the effects of urokinase therapy arises from the fact that spontaneous resolution does occur by the lung's unassisted fibrinolytic system.[7] From such observations it is logical to assume that given enough time the vast majority of pulmonary emboli in acute conditions would resolve spontaneously. If it were otherwise there would be many more patients developing pulmonary insufficiency secondary to acute thromboembolism than we actually find. It is only in the acute case where rapid lysis of clot is necessary to save life that the normally occurring fibrinolytic mechanism in the lung receives vital assistance from urokinase.

It is clear from Sautter's experience that all patients with massive pulmonary emboli in shock and those in whom inferior caval ligation is usually recommended for the prevention of further embolization should be treated with urokinase first. This enzyme, however, is not yet available for general clinical use. Two pharmaceutical houses, Abbott Laboratories and Sterling Winthrop Laboratories have produced enough urokinase for a cooperative study under the direction of the National Institutes of Health to be carried out in five different medical research centers. There is very little doubt that Sautter's results will be confirmed and amplified on a larger scale at which time production of urokinase should increase to make it more generally available.

Some investigators will now doubtless begin to evaluate the use of urokinase in arterial thrombosis. We may, however, predict with some assurance that since the white thrombus in arteries[8-9] is not built on a fibrin base, that urokinase efficiency in such cases would be minimally if at all effective. However, thrombosis on a prosthetic cardiac valve is probably of the red variety and here beneficial results might be expected from urokinase therapy.

L.H.N.

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Amandatine: Chemoprophylaxis For Influenza Virus A_2 Infection

On October 18, 1966, the U.S.F.D.A. approved the antiviral drug amandatine hydrochloride for prescription use. The only indication for the use of this drug is in the prophylaxis of influenza due to A_2 virus strains. Amandatine has no therapeutic properties and it is ineffective once the virus has penetrated the cell. The available evidence indicates that this drug offers additional means for reducing the morbidity due to A_2 influenza strains. But some questions and issues have been raised which the Council on Drugs has undertaken to answer.[1]

One is whether the expressed doubts concerning the utility and safety of this drug and the possibilities for its abuse should limit its availability. It must be acknowledged that fears of possible abuse are not entirely unfounded. Its value is only prophylactic against A_2 influenza virus infection not against influenza-like illnesses and there may be extensive casual use of it in people who have been exposed to a common cold. However, this is not a reason for not employing the drug but imposes upon the individual physician responsibility to evaluate the need for amandatine when a patient has been exposed to influenza virus A_2.

In most instances physicians will prefer to provide immuno prophylaxis with a vaccine when sufficient time is available. But supposing there is not sufficient time or supply of specific vaccine is lacking. In such circumstances chemoprophylaxis with amandatine would seem appropriate. Likewise even in patients that have received influenza vaccine, use of amandatine would seem to be justifiable in view of variable results obtained so far with the vaccine.

The number of patients tested in most individual studies has been small but the preponderance of favorable results is impressive. A theoretical point has also been raised that amandatine may enhance viral replication in man because it does this in ferrets. However, results of many laboratory studies confirm the activity of amandatine against A_2 subtypes of influenza virus in man and animals other than ferrets and does not enhance viral replication.[2]

Another question that has been raised is whether the use of amandatine will permit emergence of resistant viral strains. The council after examing all the evidence concludes this is probably not true. The council points out that although controlled field studies with amandatine would be desirable, nevertheless it would be fraught with great difficulty because this illness represents such a small part of the total respiratory disease burden of the population. Further, influenza unlike measles or mumps lacks distinguishing clinical features that would make it possible on the basis of clinical observations alone to conclude that a given patient has influenza and not a common cold. Perhaps these mechanical problems will some day be solved.

Amandatine has demonstrated efficacy in reducing morbidity due to A_2 influenza by 50 per cent and it has a low incidence and relatively mild and transitory side effects with the recommended daily dose of 200 mg. either when given all at once or in two divided doses.[3] Thus currently it can be considered a useful addition to the physician's armamentarium. Of course the physician is alone responsible for the use of the drug and must guard against its abuse. In times of a demonstrated influenza A_2 epidemic, the use of amandatine with or without vaccine would be a reasonable prophylactic procedure and would seem to be indicated specifically for high influenza A_2 risk patients of all ages. Especially if a shortage of A_2 vaccines should occur would amandatine be a particularly fortunate agent for use.

The drug may well be the forerunner of a new pharmacologic class of antiviral agents which will have profound clinical significance. Like sulphanilamide even if its period of usefulness in clinical medicine is brief, it may contribute importantly to our knowledge of viral disease control. Admittedly further studies need to be made, but the council sees no justification for restricting the use of amandatine by physicians.

There are adverse reactions which occur in about 1–2 per cent of patients consisting of gastrointestinal and central nervous system symptoms but the disturbances appear to be dose related effects and disappear on withdrawal of the drug. If the drug is kept to 200 mg. per day the chances of a reaction are slight. No renal, hepatic, bone marrow, or other hematologic disturbances have been observed in animals or reported in man.

Pharmacodynamic studies of the absorption, distribution and excretion of amandatine have shown that it is almost completely absorbed from the gastrointestinal tract and that 86 per cent of a single oral dose is recoverable unchanged in the urine. Intensive investigations have revealed no evidence of metabolites in the human urine. The half-life of the drug in man is estimated to be twenty hours. Very little amandatine is excreted in the feces and practically none in the expired air.

Amandatine apparently acts to impede the penetration of the influenza A_2 virus into the host cell. Although this effect is not complete it is sufficient to reduce significantly the morbidity resulting from exposure to type A_2 influenza virus. The exact mode of action still remains to be determined. It does not appear to affect the absorption of virus on cell surfaces nor does its antiviral effect seem to inhibit antibody synthesis completely. The drug does not exert a virucidal action. Clinical studies also reveal that amandatine is effective only if it is present in the tissues prior to their contact with the influenza A_2 virus. Once the disease has begun it signals the entry of the virus into the cell and amandatine is no longer useful.

L.H.N.

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The Conquest Of Hemolytic Disease Of The Newborn

In 1939, Philip Levine[1] described the case of a woman who had recently been delivered of a stillborn infant and because of hemorrhage had been transfused with her husband's blood. She developed a hemolytic reaction. Dr. Levine pondered over this reaction and hypothesized that the patient may have become sensitized during pregnancy and developed an antibody to an unknown blood factor in the red cells of her infant which was foreign to her but inherited by her baby from its father. In the next two years several additional intra group hemolytic transfusion reactions were discovered. Levine then observed that some of these occurred in women who had given birth to infants with edema, or anemia and jaundice. It was then that he postulated that an unusual maternal antibody against a red cell agglutinogen of the fetus could cross the placenta, destroy fetal blood and produce the disease long known as erythroblastosis fetalis.[2]

If this hypothesis is true then there is a new blood factor in the fetus hitherto unknown against which the mother forms an antibody. Since one can by passive immunity prevent the hypothetical immunization of the mother, it should be possible by passive immunization of the mother to prevent the large fetal wastage involved in erythroblastosis fetalis. The hitherto undiscovered agglutinogen, essentially a new blood group factor was named the rhesus or Rh. factor and the agglutinin developing

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in the sensitized Rh.—negative person was called the anti-Rh. antibody. This started exciting new chapters in hematology, in neontology and intra-transfusion therapy.[3]

In the following period methods were developed that detected more than a hundred new blood factors in addition to the original few and transfusions became possible with safety for millions of patients. But the danger of sensitization of the Rh.—negative woman bearing an Rh.—positive infant remained an unavoidable hazard.

The idea of passive immunization has been known since 1908, namely that passive immunity can block active immunity. In 1960, Freda[4] put this principle to use and initiated a program to determine whether initial immunization of Rh-negative mother by an Rh of fetal origin could be prevented by the passive administration of Rh antibody immediately after childbirth. At the same time and quite independently Finn, Clarke et al[5,6] began similar studies in Liverpool. The idea was to develop a feasible and safe method of obtaining passive immunity to Rh. The next step was to confirm that the immunosuppressive phenomenon by passive antibody administration to the Rh-negative mother, would be as effective in the Rh system as had been observed in other antigen-antibody systems. If so then to try immunosuppression in mothers who ran the risk of Rh sensitization.

For reasons of safety, Freda decided to use Rh containing gammaglobulin rather than the antibody containing plasma to provide passive immunity. This led him to choose fraction II. gammaglobulin made from a pool of high-titre incomplete anti-Rh donor plasma. The material was prepared and packaged by Ortho Research Foundation, Raritan, New Jersey in 1961. It was found safer to give it I.M. rather than I.V. and was found completely free from side-effects and hepatitis. After obtaining encouraging results in Rh-negative male volunteers given Rh-positive red cells they proceeded to give anti-Rh gammaglobulin to Rh-negative women recently delivered of ABO compatible Rh-positive infants and they found the same protective effect.

In Liverpool, England, Dr. Finn and Clarke and their associates had noted as had Levine previously the protective influence of Group A and B hemagglutinins in Group O Rh-negative mothers of Group A or B Rh-positive infants. They tried to duplicate this protective effect by the use of Rh antiserum as a "blocker" of sensitization. When this proved effective they likewise turned to gamma globulin concentrate of anti-Rh serums and clearly demonstrated that immunization at or after delivery of the Rh-negative woman is preventable.

Freda's first trial on Rh-negative women was begun at Columbia in 1964. They treated 180 women with Rh immunoglobulin and kept another 117 as untreated controls. Their results clearly indicate that an Rh immunoglobulin preparation works exceedingly well. Whether or not the same degree of effectiveness (100 per cent) achieved in the post-partum period will persist throughout a second or subsequent pregnancy still remains to be determined. Thus far the second pregnancy results are most encouraging.

As soon as this preparation becomes generally available as a public health measure for the prevention of hemolytic disease of the newborn we should begin to obtain widespread experience of its benefits in second and subsequent pregnancies. We can say now, however, that a great step forward has been taken. In another generation the danger that hitherto has threatened the child bearing potential of about 200,000 women per year in this country alone, should have been removed. The treatment hitherto used of intrauterine transfusion and exchange transfusion will become of historical interest only.

As immunology marches on the next great advance should be the neutralization of preformed antibodies in a wide variety of auto-immune disease. It is not difficult to imagine the untold benefits that will result once this has been achieved.

L.H.N.

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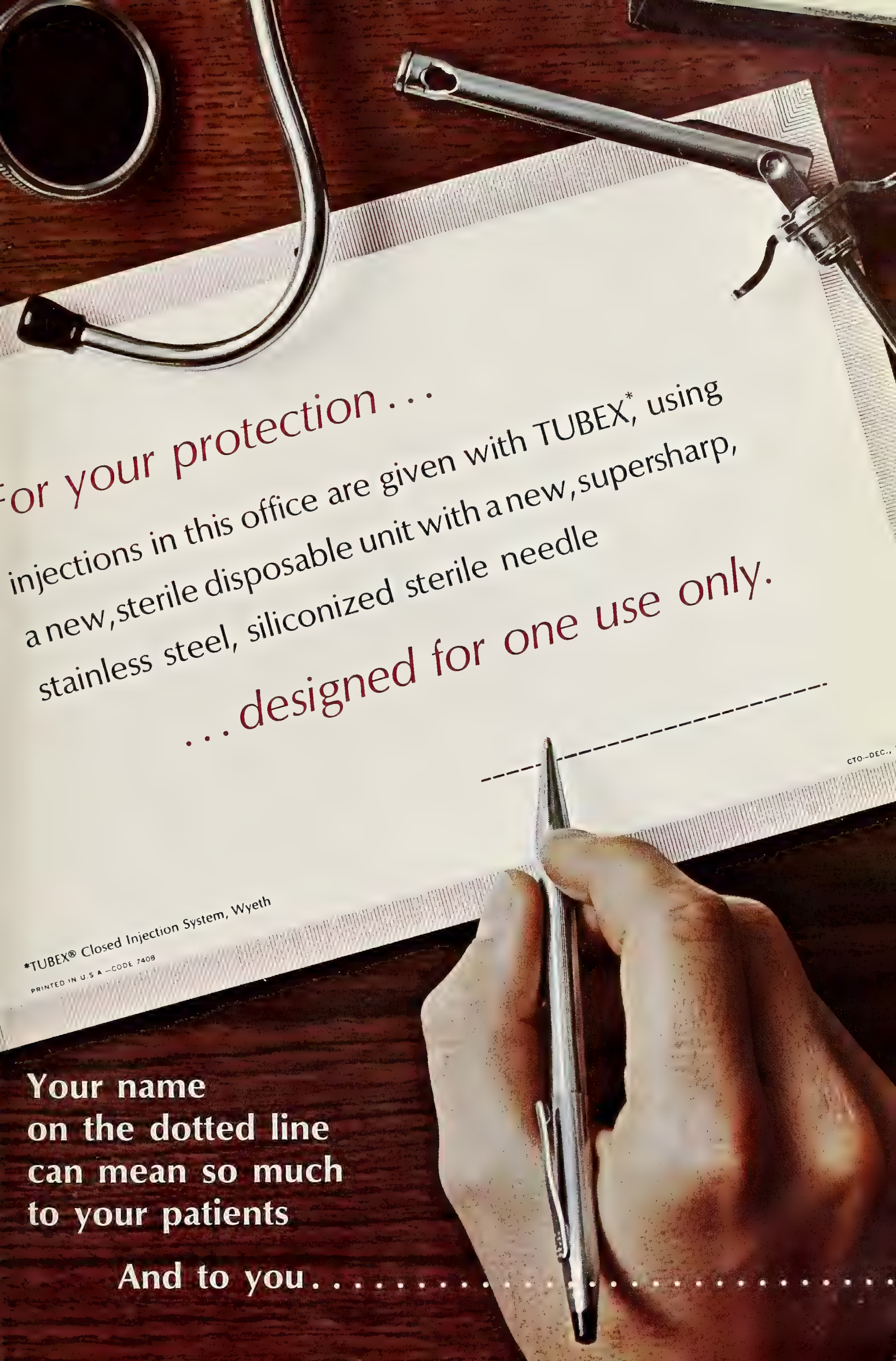

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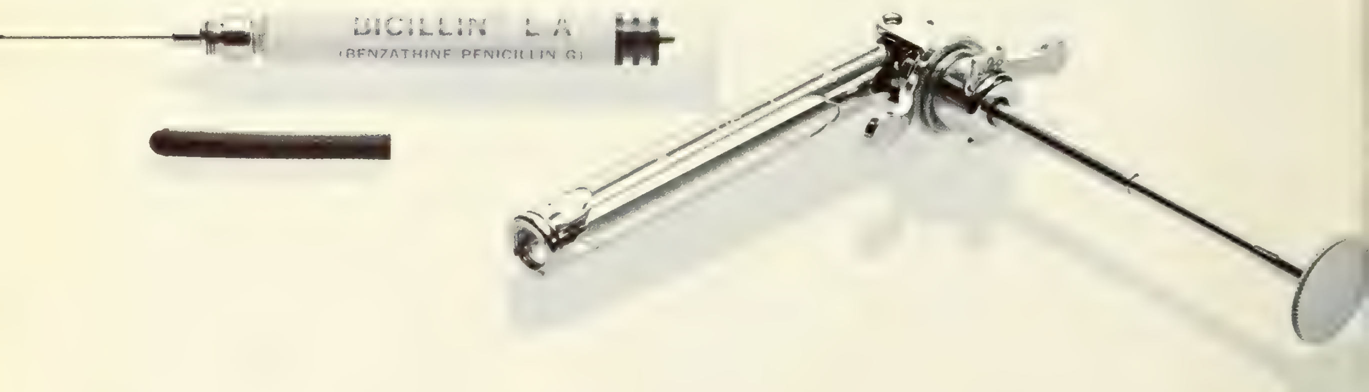

Hemotherapy Now And In The Future: I.

We all know what the ideal kind of blood for therapy should be. It should be readily available and safe. That is, it should be completely compatible, free from the danger of hepatitis or of any hazard whatever of early or late transfusion reactions. It should be capable of surviving in the new host as long as it would have survived in the donor and capable of fulfilling all the normal functions. Obviously there are only two possible sources of such ideal blood for any of us; an identical twin of whom there are too few and every one of us himself. The precedent for the latter has already been established by surgeons who favor drawing a unit of blood from patients with normal hemoglobin levels a few days prior to selective surgical procedures and returned to the patient during operation. Surgeons have also returned blood from the peritoneal cavity to patients who have lost it. There are also cases on record in which blood donated by volunteers was transfused back to them when they unexpectedly needed it themselves.[1]

Autotransfusion then is the ideal way of giving blood to a patient and what is necessary is a successful method of blood preservation. Advances in cryobiology have made it possible to preserve blood for a long time. When frozen blood stored at –80 C. is used after many months later on the original donor, it is less antigenic, less likely to cause isosensitization and has a 65 per cent or greater post-transfusion survival.

Immunologic obstacles have limited the use of homologous bone marrow in patients who have been treated with drug or radiation for a variety of cancers and leukemias. Difficulties so arising could be eliminated by using ones own marrow. Just as red blood cells could be deposited and kept for years for our own needs so could bone marrow. Both in the case of red blood cells and bone marrow repeated deposits could be made to provide an adequate supply without harm to oneself. Autotransplantation of frozen stored marrow has been tried first in animals and then in patients with cancer, in order to protect them against large doses of radiation. The transplanted marrow cells grew and proliferated in recipients. Marrow kept frozen for long periods retained its protective ability.

Marrow was aspirated and after drug or radiation treatment was returned by intravenous injection. The evaluation of this form of therapy was difficult because of differences in the reactivity of the host to radiation and cytotoxic drugs. Thus far the protective ability to transplanted marrow was found higher in patients subjected to whole body radiation than in those subjected to cytotoxic drugs.

Good methods for marrow preservation are already available. Fifty per cent of the myeloid and erythroid stem cells in the marrow survive freezing preferably in from 10–15 per cent of dimethylsulphoxide. We already know that antigenicity was reduced in skin stored at –60 C. and yet its viability was well preserved. If marrow reacted similarly then transplantation would be easier. It has already been shown that granulocytes, lymphocytes and megakaryocytes survive freezing. With further improvement and simplification of equipment and methodology, red blood cells and marrow may come to be preserved indefinitely at least for all practical purposes. When that happens one will be able to deposit one's own blood and marrow for use when he himself will need it.

There is another possibility and that is marrow culture. Human epithelial cells, normal and abnormal, may now be grown in tissue culture in large amounts to supply investigators and others using such materials all over the world. There are some difficulties in growing marrow cells in vitro but it is reasonable to assume that eventually practical methods will be found to grow various marrow cells in culture. In fact we may be nearer to this realization than successful transplantation of other organs.

The possibility of having available growing and multiplying cultures of one's own marrow cells for personal use is not a topic merely for science fiction. It is almost at hand. It should not be long before we succeed in growing megakaryocytes in the test-tube and in having them produce platelets. The same method once perfected may be applied to the cultivation of one's own granulocytes, to the treatment of agranulocytosis of whatever origin. Such an advance in tissue culture will make the use of blood components even more applicable than it is today. In fact the time should come when the first deposit of one's own blood for preservation and future use may begin at birth, the blood being drawn aseptically from the placenta.

The possibility of providing a supply of one's own plasma for one's own future use is already available for every one of us. Nothing new stands in the way of having several units of blood drawn, returning the cell mass to the circulation by means of plasmapheresis and depositing the plasma for future use. This method would provide reserves free of the danger of hepatitis. Advances in cryobiology, already achieved, justify the hope that whole blood also will be drawn and stored and preserved for future use. This storage would not require much more space than are occupied by safety deposit boxes in a bank.

L.H.N.

(references after second installment)

Leg Vein Thrombosis

Leg vein thrombosis is a serious disorder because of its frequent termination in pulmonary embolism which may be fatal. A large literature has grown up since Virchow[1] first outlined three factors in thrombosis, a change in vessel wall, a change in rate of blood flow, and a change in the composition of the blood. What is the relative importance of these factors? Many studies have been reported to support each of these factors. Then there are others. What is the relationship of thrombosis to phlebitis? How do thrombi propagate? What is the site of origin of thrombi and is there any special explanation for their occurrence in selective sites? These questions all have broad implications with respect to diagnosis, prophylaxis and management.

There are some important aspects of the anatomy of the veins in the legs that we need to be conversant with besides the names and locations of the major veins and their numerous unnamed branches. One is the rich venous plexus within the soleus muscle which is not described in the standard anatomy textbooks, but which has been studied in great detail and is important in the question of thrombophlebitis. The anatomic structure in the veins of the leg have been sited as sources of pressure causing decreased flow and stasis which is a recognized important factor contributing to thrombosis.

The soleus muscle compresses the posterior tibial vein. The inguinal ligament compresses the femoral vein. The intramuscular veins like the soleus plexus depend for their emptying on muscular contraction. The veins are thin walled and easily become distended by a stagnant column of blood and this perhaps explains the high incidence of thrombosis found in these intramuscular veins. Several investigators have found thrombi more frequent in the left leg than in the right and have attributed this to another anatomical factor, the compression of the left common iliac vein by the right common iliac artery as well as to pressure by the rectosigmoid colon on this vein. The prevention of constipation would therefore seem logical in such patients.

The study by Stein and Evans[2] using post-mortem venography helps to point up many of the factors involved in venous thrombosis. Their study was done on unselected cases together with gross dissection and microscopic examination in order to assess the incidence, location, point of origin and mode of propagation of venous thrombi in the legs. Post-mortem phlebograms are very reliable for detection of antemortem thrombi in the veins of the thigh also. They readily reveal collateral channels, dilated valve pockets and readily aided the authors in the location of thrombi by dissection.

Their incidence of leg vein thrombosis was about as described from other large series, not quite 50 per cent, 13 out of 27 patients. Twelve were in calves. Thrombi large enough to cause significant pulmonary emboli were found in one-fourth of the patients and all who showed pulmonary embolism at post-mortem. Careful dissection showed that initiation of thrombosis occurred both in thighs and calves. Valve pockets were a frequent site of origin of thrombi. Inflammation in the wall of veins occurred in only one patient and this was found to be secondary to the thrombosis. Propagation of thrombosis was studied by the authors and they found both forward and backward propagation, though the forward thrombosis seemed more common.

The early view that thrombosis is a result of phlebitis is not supported by this study. It is true that Virchow found cellular reaction in vein walls, but this reaction, unless due to trauma, usually does not appear until after the thrombus has been laid down. When thrombosis in leg veins have the clinical signs of inflammation; warmth, swelling, tenderness, a clinical diagnosis of thrombophlebitis is often made. When no sign of phlebitis is present and pulmonary embolism occurs it is termed phlebothrombosis.

The histologic evidence of many workers, supported by Stein and Evans, however, do not support the sharp distinction made clinically between phlebothrombosis and thrombophlebitis as for example following mechanical or chemical injury, but these latter are very rare as compared with the incidence of thrombosis without inflammation. We need to remember that a thrombus can

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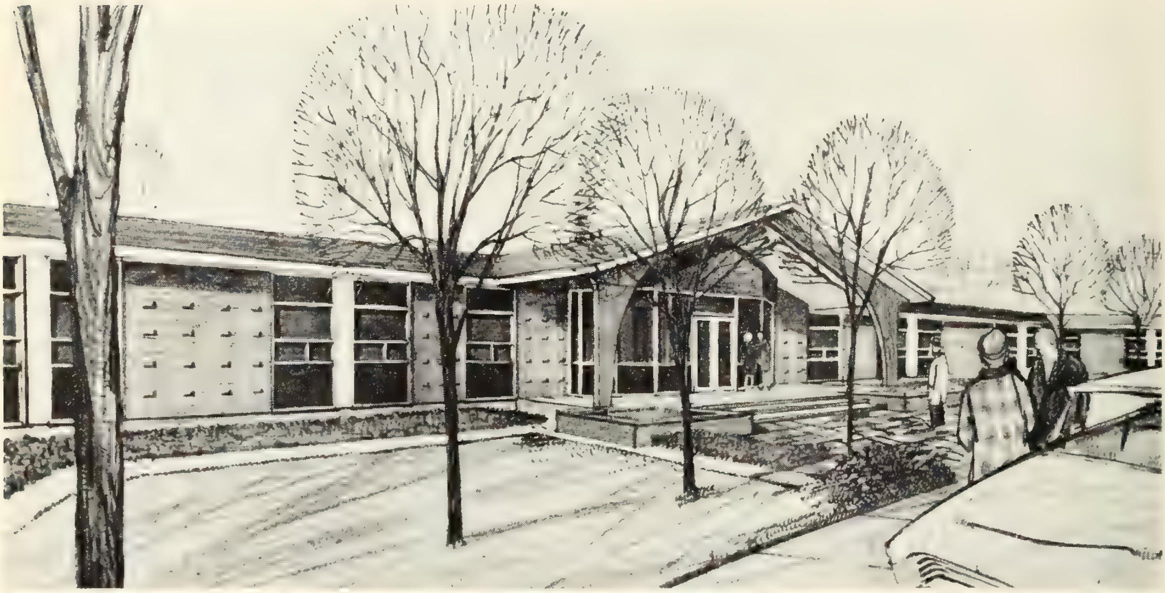

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induce inflammation in the underlying vein wall and may be extensive enough to cause tenderness, swelling, and fever compatible with the clinical diagnosis of thrombophlebitis. However, the underlying pathogenetic mechanism is primary thrombosis and not primary phlebitis.

As noted above only one case in Stein's series had clinical thrombophlebitis but at post-mortem the inflammation though present was secondary to thrombosis. In fact pulmonary embolism occurred in thrombosis cases and fatal pulmonary embolism also occurred in patients with clinical evidence of thrombophlebitis. Thus there is no clear evidence to indicate that inflammation of the veins prevents thrombi from embolizing or that embolization is any more frequent in patients with leg vein thrombi not associated with venous inflammation.

The conclusion is warranted that thrombosis of the lower limbs as seen in this era of medicine usually occurs without inflammation and that inflammation when associated with thrombosis is usually secondary to thrombosis and that the likelihood of embolization is high in patients with as well as without inflammation associated with leg vein thrombosis. We need to bear in mind the anatomical factors contributing to stasis and work to avoid them and we need to combat the hypercoagulable state which contributes to the development of the red thrombus.[3]

L.H.N.

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New Livers For Old

Many patients have had considerable prolongation of life by virtue of chronically functioning renal homografts. In Starzl, et al.'s[1] experience more than 50 per cent of the patients treated are still alive one and a half to three years after operation, having had continuous urine excretion by their new kidneys during these intervals. In view of such encouraging results interest has mounted that homotransplantation may be an effective technique for the treatment of various diseases that affect primarily a single organ system that has suffered functional failure.

At present liver transplantation appears to offer the most immediate possibility of clinical utility. Many patients die with hepatic failure or hepatic carcinoma and a sober look at the problem of homotransplantation of the liver is in order. From experiments on dogs arises the principle hope that homotransplantation of the liver may some day be a practical undertaking.

To test the problems involved in successful liver transplantation Starzl, et al. excised livers from one dog and transplanted it into another. The recipient liver was removed and replaced with a normally revascularized homograft. In this kind of an experiment, there can be no argument about the presence or absence of transplant viability because the proof of viability is provided by the continuous function of the organ. The procedure was attended with a relatively low immediate mortality of 10 per cent or less. If untreated, the homograft undergoes rejection within seven days, a process similar to that observed with other tissues and organ transplants. In addition to rejection, there was also the great variability in response of the animals to the homograft.

The most effective agent for mitigation of rejection has been azathioprine. Unfortunately this drug is a hepatotoxic agent which even in small doses causes acute liver injury in the majority of animals within a few days after beginning administration. This high degree of toxicity is apparently specific for the dog. The hepatic dilemma is evident, since at present it is necessary to use a liver poison to prevent the effects of liver rejection. It is true that azathioprine is less hepatotoxic in man, nevertheless several cases of "hepatitis" have been observed in humans treated with this agent long after renal transplantation.

In spite of this handicap long-term survival has been obtained after orthoptic liver transplantation in the dog. In a recently reported series of nearly 100 liver homotransplants, the potentiation of homograft function obtained was comparable to that reported after homotransplantation of the dog kidney. The four longest survivals are now over one year with a maximum of twenty months.

Then there was the question of great variability of response of the animals to the homograft. About one-fifth of the dogs being treated with azothioprine alone had some clinical evidence of rejection although their transplants in general had little histologic change when biopsied many months after operation. At the other end of the spectrum approximately one-third underwent overwhelmingly immunologic repudiation of their homografts, leading to liver failure and death in one to six weeks and this in spite of comparable therapy.

Finally, in half of the animals evidence of some rejection was present at times to a very severe degree but with ultimate partial or even relatively complete reversal. In this last group improvement in homograft function occurred without intensification of the pre-existing immunologic regimen. This provides strong evidence of an important principle namely that homograft rejection has a tendency to spontaneous remission.

How do we explain the great variability of these results? Certainly there must be differences in the quality of chance histocompatibility matching between the donors and the recipients, a problem similar to that which exists also in the human population. And this points up the need for preoperative identification of histocompatibility between donors and recipients, if we are to be able to give some predictability to the results before, not after, either experimental or clinical operations of this type.

We are in great need of practical methods for such antigen analysis which as yet are not available although many investigators are actively exploring this area. The real question however remains. Where are the livers to come from to save a patient whose liver is destroyed. Will it be a cadaver, a chimpanzee, or what?

L.H.N.

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Dopamine And Parkinson's Disease

Two catecholamines are now recognized as physiologically active substances both in vertebrates and invertebrates, norepinephrine and epinephrine. To these has now been added dopamine. The outcome of a search that has stretched over twenty-seven years and a half dozen countries is the discovery by which the sympathetic nerve transmitter norepinephrine is made by nerve cells from a dietary amino acid tyrosine which is converted to dopamine which in turn is finally oxidized to norepinephrine. The idea that dopamine is not just an intermediary in the formation of norepinephrine but an active amine in its own right was made clear in a program arranged by the Parkinson's Disease Information and Research Center at Columbia University and reported by Campbell in Science.[1]

The neuropathologist Abner Wolf said at the Symposium that degeneration and disappearance of melanin and dopamine containing cells in the substantia nigra is the only pathology that has been constantly demonstrated by post-mortem studies of patients with Parkinson's disease. This suggests that degeneration of a nerve pathway from the substantia nigra to the forebrain motor centers causes Parkinson's disease by depleting the forebrain motor centers of dopamine. In fact four main findings pointing to dopamine as the compound in the brain needed to prevent this disease and whose absence leads to Parkinson's disease were the highlights of the symposium.

One was that there exists an almost complete lack of dopamine in the forebrain and motor centers of patients suffering from Parkinson's, centers where it is normally highly concentrated. This report by Hornykievicz from Vienna was based on a study of forty brains of patients with Parkinson's disease. He compared the dopamine content of these patients with brains of patients who did not have this disease.

The second line of evidence was reported by Carlsson who found a high concentration of dopamine in the same forebrain motor nuclei in a number of species of animals. He expressed his surprise at finding dopamine in the brains of normal animals in about the same quantities as norepinephrine. This lent support to the view that dopamine might have a function of its own apart from being merely a precursor of norepinephrine.

A third line of evidence was the finding of a high concentration of dopamine in the nerve pathways connecting some forebrain nuclei with the largest nucleus of the human midbrain, the half-moon shaped dark colored substantia nigra. Dopamine also extended in high concentration inside the nerve fibers which originate in the cell bodies of this nucleus and extend to their terminus. A new technic which converted dopamine to a fluorescent complex made this discovery possible. Two smaller dopamine containing pathways were thus uncovered one of them terminating in a nerve network at the pituitary gland and is "probably involved in the control of anterior pituitary secretion."

The final link in the evidence was to deplete the forebrain nuclei of its dopamine by severing the

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nerve pathways linking the substantia nigra to the forebrain nuclei. One should therefore also be able to produce Parkinson's disease in animals and humans by drugs that deplete brain concentrations of dopamine. This in fact has been reported in animals placed on reserpine and phenothiazines. It is also a well recognized sequel in humans who have had prolonged administration of these drugs. The most effective drug to produce such symptoms was described by Guy Everett of Abbott Laboratories as tremorin, a powerful depleter of dopamine content of the grey nuclei of the corpus stratum and subcortical mass of grey and white matter lying above the thalamus in each cerebral hemisphere.

The dopamine findings mean progress, but the complexities of the problem are still immense. We do not know how the neurochemicals fit into the fantastically complicated efficient structure of the nervous system. Furthermore although dopamine is in high concentration in the nervous system, it is also an important amine in the adrenal, intestinal tract, lung, liver and heart and accounts for as much as fifty per cent of the catecholamine content in certain other organs.[2] It seems to have important functions in the periphery as well. Prasad and Van Woert have found it highly protective against whole body irradiation, but it must be administered to the experimental animal before the exposure.

Added import to these dopamine findings is the increasing hope for improved chemotherapy of Parkinson's. There are an estimated one million persons in this country suffering from this disease. We have seen it only as a clinically descriptive entity, but now we have made an opening through basic studies of cell function. We see how drugs produce it and we have good reason to hope that work such as was reported at the Symposium will lead not only to chemical cures of Parkinson's disease, but will uncover other physiological processes dependant upon dopamine.

L.H.N.

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The Search For The Exceptional Animal

When man changes to a more abundant diet especially an increase in carbohydrates this tends to bring out diabetes in a population in which it was previously unexpressed. This is found in immigrants to Israel. It is true for Indians who immigrate to Africa. In India diabetes is rare, in Africa it is common. The animals for studying the diabetic state heretofore have been depancreatized or given alloxan. These, however, do not provide the opportunity to study the gradual development of the disease. We need an unusual animal who like man develops diabetes by overeating.

Quite by accident such an animal turned out to be the sand rat. He has an unusual kidney having only long looped nephrons. He can produce a more highly concentrated urine than any other mammal. He seemed made to order for study of the role of the loop structure in the renal concentration mechanism. However, this animal was a real nuisance to breed, because it developed diabetes and could not reproduce. When it grew fat and diabetic he had a high plasma insulin level and therefore its diabetes was due not to an insufficiency of insulin but to interference in the peripheral action of insulin. All in all because of a simple caloric overabundance the sand rat displays the full pathology of adult human diabetes.

The similarities between the development of diabetes in man and the sand rat seem to make the latter an admirable tool for study of the development of the diabetic condition since otherwise one needs depancreatized or alloxan animals and these cannot provide opportunity to study the gradual development of the disease. The fat sand rat is in a way designed for studies of the relationship between a more than adequate diet, obesity and early changes of the prediabetic and diabetic condition.

One of the earliest examples when an exceptional animal offers a unique opportunity for the experimenter is that of Priestly, known for his discovery of oxygen, who wrote to a French chemist friend that he obtained the purest nitrogen, more pure than he could prepare in his laboratory by going to the London fish market buying carp and using the gas in the swim bladder.

In this century there are other examples. Everybody knows Drosophila the fruit fly which in summer swarm around an overripe melon. Morgan in 1910, at Columbia, looked around for a suitable object for genetic studies and observed some of

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(potassium phenoxymethyl penicillin) Wyeth these normally red-eyed fruit flies had white eyes. Soon he noticed that it was always males that had white eyes except when there was a double dose of the genetic trait.[1] This discovery of the sex linkage led to the famous discovery of chromosome linkage of the genes and the spectacular development in genetics in the next fifty years. From this, his student Sturtevant saw the possibility of determining sequences in the linear dimension of the chromosome and then produced the first chromosome map. It would seem as if the fruit-fly was created solely for the purpose of heredity research for it reproduces itself with incredible profusion and rapidity requiring but twelve days from egg to maturity. Its cells contain only four pairs of chromosomes all of a different size and easily recognizable and besides it gives rise to a profusion of mutations. In its salivary gland it has what are known as giant chromosomes each are so large that the genes can actually be located in the visible chromosome and a complete chromosome map could be correlated with the picture seen in the light microscope—the genes had been made visible.

Many other important discoveries can also be related to the use of one particularly suitable animal. Only one animal besides man can develop scurvy due to insufficient ascorbic acid and this is the guinea pig. Otto Loewi's discovery of the neurohumoral transmission from nerve to effector organ was made on the frog. It so happened that this discovery could not have been made had he worked on a mammalian heart. Instead of blood he used saline which seems less "physiological," but had he used blood, the experiment would have been negative and the transmitter substance acetylcholine (ACH) would not have been discovered. Because the clam—venus mercenaria is particularly sensitive to ACH in addition to its gastronomic use the clam is now sought as the standard assay animal for ACH.

Another well known animal which is eminently suited for a particular assay is the firefly. Once it was discovered that the light of the fire depends on luciferin, the enzyme luciferase and the amount of ATP present, then the firefly could be used in the assay of ATP. It is so much easier and more accurate to measure the quantity of emitted light than to determine in any other way the quantity of ATP. The use of the firefly in fact is the most elegant and flashiest example of a bio-assay.

There are several aglomerular fishes which can be used to determine whether glomerular filtration is necessary for life in fresh water—kidneys without glomeruli. Lophus piscatorius, an ugly flattened fish mostly mouth has kidneys without glomeruli. A Malayan pipefish similar to fresh water animals is reported to have no glomeruli. No physiologist has yet taken up this challenge.

All we know about the mechanism of conduction in the nerve fiber is derived from the studies of the giant axone of the common squid. These axons control the swimming of the animal which takes place by jet propulsion. When the muscular mantle contracts a jet of water is forced out through the siphon. For the entire mantle to contract at once, the nerve impulse must reach all parts at the same time. The most distant parts are served by the thickest fibers in which conduction velocity is the greatest. A single giant axone may be almost a mm. in diameter with a cross section 100—1000 times greater than a single mammalian fiber. These axones were not easily discovered because they are no more than four to five inches long.

In further development of neurophysiology three important events stand out. One is the voltage clamp method. Then there is the perfusion method which demonstrated that a nerve can still conduct after the inside has been squeezed out and replaced by a salt solution. A third important development depends on a poison known as tetradotoxin, a poison from the puffer fish which is a highly specific inhibitor of sodium movement. This permits the separation of electric phenomena in nerve conduction due to sodium and those due to other cations.

Another biologic specimen, the giant barnacle (Balamus nubilus) a pacific species contains single muscle fibers which are 10 cm. long. It is insensitive to tetradotoxin. Some salamanders and newts are likewise insensitive to tetradotoxin while others are extremely sensitive and become paralyzed. Thus of great interest to nerve and muscle physiologists is that a potent toxin should occur in two unrelated groups of vertebrate, the puffer fish and one group of salamanders.

Besides unique similarities there are also striking differences in behavior in two closely related species. The guinea pig uterus is extremely sensitive to histamine, the rat uterus is insensitive. The guinea pig can therefore not be used for assay of oxytocic activity in extracts from the neurohypophysis because it is frequently contaminated with histamine, the rat uterus however can be so used.

The animals so far discussed exhibit unique characteristics which make them singularly suited

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for specific scientific purposes as if the animal had been designed for this purpose in mind. And yet these animals are no more unique than many others. Unusual animals are all around us right there "in the bush" ready for the open eye and keen mind. One such animal not yet used provides an exceptional easy access to the embryo at a very early stage. For example in the red kangaroo the newborn embryo weighs only 750 mg. when it enters the pouch. This tiny blind underdeveloped young appears at the birth opening and swims for fifteen to twenty minutes through the wet fur that the mother has moistened with saliva. It ends up in the pouch where it grasps the nipple which then swells up inside its mouth so that the helpless young remains attached and is provided with milk. Here one can have access to a fetus before its immunologic mechanisms become functional. By being able to reach the embryo this early, one should be able to design to order the immunologic makeup of the individual. This easy access could be valuable for a wide variety of other purposes where an early access to the underdeveloped organism is of importance.

There is one other extraordinary animal, the armadillo which as far as is known has not at all been used for what seems its designated purpose. The armadillo always bears quadruplets and these are always identical. Identical twins are a much sought research tool, but not terribly common. Identical quadruplets are most unusual. But since in the armadillo, the quadruplets are invariably identical, we can say that here again we can always expect the unexpected.

L.H.N.

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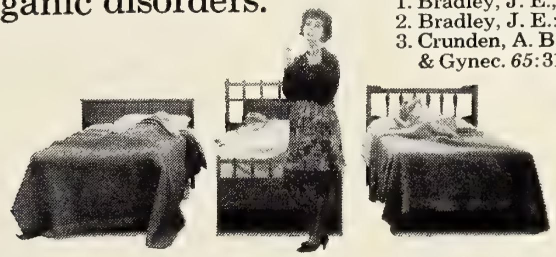

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Some Sociologic Effects Of Medical Discovery

In 1926, Alexander Fleming noticed the inhibitory effect of a fungal contaminant on the growth of a culture of a staphylococci. This observation led to isolation and purification of penicillin and opened up a new era of antibiotic therapy and the control of infectious disease. In 1965, Public Law 89–97 set in motion the experiment in social medicine known as Medicare. Is there a link between these apparently disparate events? There is and we would do well to gain insights into it for each action in medical discovery leads to a social action as well including often moral and ethical considerations.

Pneumonia was a major killer and "the old man's friend." In a few relatively merciful days, the patient used to be spared months of hopeless illness. Now his life is saved by penicillin to become a senior citizen. Living, like dying creates problems for society, more pleasant but still problems. Now the problem created by antibiotics is a large and increasing population of old and unemployable citizens subsisting marginally on retirement and social security payments. The simple economics of their existence has effected a revolution in the public's conception of the proper role of Government in the lives of men. The passage of Medicare suggests that more has changed than the public's attitude towards big government. The American people have developed a new concept of health itself. They have come to consider health as a civil right guaranteed under the "pursuit of happiness" clause of the Declaration of Independence.

This belief that health is a human right is new in the American scene. It is new because people now believe that medicine can cure or arrest disease. Formerly illness, suffering and death were facts of life. When illness struck, both patient and doctor relied on nature's help. Now for the first time in history physicians are actually dealing with specifics in medicine: specific etiology, specific diagnosis, specific treatments. People now are used to medical miracles, new ones are arriving every day and it is not surprising that patients should come to view health as a right.

The miracles as well as their aftermath are expensive both economically and socially. As antibiotics eliminated death from infections, people lived longer and reached the age when they were subject to chronic diseases. Now cancer, heart disease, and strokes joined poverty as the prime enemies of the "great society." To wipe them out we are in the process of establishing regional health centers dedicated to investigation and treatment of these categories of disease. These regional medical programs will almost certainly alter the nature of practice more than will Medicare. This then is another consequence of medical discovery.

All the social effects of penicillin are too numerous to mention or even to know. On the economic front Life Insurance Companies accumulated fortunes operating on pre-penicillin actuarial tables. Pharmaceutical companies were allowed unique margins of profit on the strength of their plea that creating miracles is an expensive business. Daily the germ plasm pool is contaminated by the medical salvation of genetically blighted children who formerly died before reproducing.

To be sure no one would claim that the widespread use of penicillin alone produced the social changes just recounted. Life expectancy was increasing before penicillin from improvements in sanitation, nutrition and housing and reduction in fatigue. Other factors may be involved in the mounting death rates due to cardiovascular disease and cancer. It may also be doubted that the simple existence of more older people has led this nation to see great merit in the looming mammoth centralized welfare state. The point is that many medical advances while clearly beneficial to man also shared in the creation of serious social problems.[1]

At this moment we know nothing about the ill effects future generations may expect from the harmful genes perpetuated by today's medicine. The few biological scientists who have shown concern have been singularly unsuccessful in preventing the development of agents of chemical and bacteriological warfare that could have a destructive capacity equal to that of nuclear weapons, and as the facts become known, the staggering increase in the effects of iatrogenic disease[2] could become a matter of great concern.

How then does one cope with the social problems of medical discovery? When cancer and heart disease are obliterated how will man manage to die? Can we count on highway accidents, nuclear holocaust, chemical and bacteriologic destruction of the germ plasm? What will we do when we are handed millions of persons living to an average age of 110? The problem is real, things are moving so fast in medical discovery we will not have time to adjust without plan as society had after Watt's discovery of the steam engine.

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Adverse Reactions: Drowsiness; dry mouth; nasal congestion; constipation; amenorrhea; miosis; mild fever; weight gain; hypotensive effects, sometimes severe with I.M. administration; epinephrine effects may be reversed; dermatological reactions; parkinsonism-like symptoms on high dosages (in rare instances, may persist); lactation and moderate breast engorgement (in females on high dosages); and less frequently, cholestatic jaundice (use cautiously in patients with liver disease). Adverse reactions occurring rarely, include: mydriasis; agranulocytosis; skin pigmentation; epithelial keratopathy; lenticular and corneal deposits (after prolonged substantial doses).

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In the world of biological science the human implications of what is going on in the sophisticated universe of tissue cultured cells, bacteria, and viruses is recognized by Sir Macfarlane Burnet as frankly terrifying. The process of evolution and the nature of man will soon be amenable to modification. There will be beneficial and harmful effects of scientific discovery. Ethical and social planning in genetics is urgently needed. Human genetic manipulation is no more than ten to twenty years away! What kind of human being do we want? It is not too early to come to grips with the social, moral and ethical problems inherent in medical advances. The task of predicting possible adverse effects of discovery must be done and a certain part of this job can be done by the scientist alone.

Biological science now faces the social and moral consequences of its startling technical advances. Shall we just continue to accumulate factual knowledge without due consideration of its effect on society and human values. Saphroglyne is the Greek ideal for self-restraint, moderation and clear vision. Modern scientific man riding "the accelerating rocket of the application of his technical knowledge and rushing on he knows not whither" needs desperately the Saphroglyne.

L.H.N.

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Magnesium—Its Nutritional And Pharmacologic Effects

Magnesium is probably one of the least understood of the nutrients which appear to be essential in man. About 20 to 40 mEq are ingested daily in an average diet, an amount which normally is more than adequate. A deficiency or an excess of magnesium can occur, however, and can produce serious clinical effects which may be incorrectly attributed to other causes. A deficiency of magnesium probably results most often when gastrointestinal fluid and electrolyte loss is treated with magnesium-deficient parenteral fluids. Excess usually occurs in patients with chronic renal insufficiency who have habitually used antacids or cathartics containing magnesium compounds.

Magnesium helps regulate neuromuscular transmission and it is essential to the activation of numerous enzyme systems, particularly those associated with adenosine triphosphate (ATP). In pharmacologic doses magnesium acts as a central-nervous-system depressant. Total body stores of magnesium in an adult amount to about 2000 bEq, more than half of it in bone. Almost all of the magnesium in soft tissue is intracellular (including that in red blood cells), and plasma magnesium concentration is normally only about 1.5 to 2.2 mEq per liter. Large changes in body magnesium stores, as demonstrated by muscle biopsy assay, sometimes occur, and they may or may not be reflected in plasma levels (J. L. Caddell and D. R. Goddard, New Eng. J. Med., 276:533, 535, 1967). Magnesium metabolism is closely linked with the metabolism of calcium and potassium, but the precise relationship is obscure.

MAGNESIUM DEFICIENCY — Deficiency of magnesium is probably more frequent than excess, and is characterized by muscle cramps and carpopedal spasm, positive Chvostek and negative Trousseau signs, and low voltage patterns in the electrocardiogram. Delirium, muscle tremor, bizarre muscle movements and convulsions may also occur.

Severe diarrhea, prolonged vomiting, and nasogastric suction (as after surgery) may lead to magnesium deficiency, especially when the patient is treated with magnesium-deficient fluids. Patients with malabsorption, regional enteritis, and ulcerative colitis are particularly vulnerable. Severe magnesium deficiency may also develop in comatose diabetic patients receiving fluid therapy and large doses of insulin. Edematous patients intensively treated with diuretics may occasionally develop magnesium deficiency. In tropical countries magnesium deficiency is common in malnourished children.

Renal loss of magnesium sometimes contributes to the development of a deficiency state. Magnesium deficiency often occurs in chronic alcoholics perhaps as the result of inadequate diet; however, alcohol also increases the urinary excretion of magnesium (L. G. Welt and H. Gitelman, Disease-a-Month, Chicago: Year Book Medical Publishers, May, 1965.)

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Foreword

This special hematology issue of *Connecticut Medicine* is dedicated to Dr. Theodore S. Evans of New Haven in appreciation for the service he has rendered to his many devoted patients and physician associates for more than forty years. Of particular interest is the fact that Dr. Evans is the first physician in our State to have centered his major medical interests in the field of hematology, and eventually to have become recognized both nationally and internationally, as an outstanding clinical hematologist.

Dr. Evans received his undergraduate education at Yale University and his medical education at Columbia University, College of Physicians and Surgeons in New York. Following several years of house officer training in Boston and New York he entered the private practice of medicine in New Haven in 1924. His subspecialty training in hematology was mainly self-taught through reading, clinical observation and association with such people as Dr. Charles Doan, Dr. Florence Sabin, Dr. William Dameshek and many others. At that time there were few fellowship appointments in any specialty areas as we know them today and the development of skills in specialty was an individual responsibility.

During the middle 1930's and through to the present time Dr. Evans has contributed a number of outstanding clinical reports to the hematology literature with primary focus on such subjects as pernicious anemia, thrombocytopenia, splenectomy, and the various leukemias. Perhaps his most notable contribution was his publication with Dr. T. F. Klumpp in the Archives of Internal Medicine in 1936 of a description of 8 cases of monocytic leukemia. Although monocytic leukemia had been described earlier it was not until this paper defined some of its more unique clinical features was it clearly established that monocytic leukemia is a distince clinical entity and different from the lymphocytic and granulocytic forms of leukemia. Dr. Evans' paper in Medicine in 1942 on monocytic leukemia is a classic in this field.

Dr. Evans has had a long and close association with Yale University School of Medicine. He was a Clinical Associate Professor of Medicine from 1937 to 1950 at which time he was promoted to full Clinical Professor. He has served as Chief of the medical service of the Grace New Haven Hospital and Hospital of St. Raphael in New Haven and the Griffin Hospital in Derby. In addition to his participation in the activities of many local and State medical organizations Dr. Evans is a charter member of both the International Society of Hematology and the American Society of Hematology.

His many students and associates join in recognition of these notable achievements and in wishing Dr. Evans continued success in his medical career.

Stuart C. Finch, m. d.,

Guest Editor

COURSE AND MANAGEMENT OF "APLASTIC ANEMIA"

Pasquale Emil Perillie, M.D.

The earliest concept of the pathogenesis of aplastic anemia was based primarily on the morphologic evidence of a pancytopenia of the peripheral blood associated with an anatomically acellular bone marrow.[1] It was concluded that the lack of cells in the circulation resulted from the physical lack of their precursors in the bone marrow. In its original description, therefore, aplastic anemia was considered an acute fulminating refractory illness resulting from an anatomical failure of the bone marrow and usually leading to rapid death by either hemorrhage or complicating infection. More recently, however, the term aplastic anemia has acquired a functional designation. Patients are seen with unexplainable pancytopenia without lymphadenopathy or splenomegaly and with a protracted course lasting from months to years. The bone marrow in some of these patients is normocellular and at times hypercellular. In a small number of patients erythroid maturation may be megaloblastic in type. In patients with normocellular or hypercellular marrows the marrow is visualized as being physiologically aplastic in that it is unable to deliver cells to the circulation in adequate numbers despite an apparent adequacy of precursors. Indicative of the newer physiological conception of "aplastic anemia" has been the variety of descriptive terms used in the literature to describe patients in this disease category. Among these terms are primary refractory anemia, toxic paralytic anemia, aregenerative anemia, pseudoaplastic anemia and idiopathic bone marrow failure[2-3].

The peripheral blood of most patients demonstrates a pancytopenia with a relative lymphocytosis. The main presenting symptoms are those of anemia. The anemia, although usually normocytic, normochromic in type may be macrocytic. An occasional patient may have a modest reticulocytosis resulting from a mild hemolytic component. In addition, in patients who have associated leukoneutropenia or thrombopenia, the clinical course may be complicated by infections or bleeding problems.

It is of practical clinical significance to note that paroxysmal nocturnal hemoglobinuria may present as a pancytopenia or conversely the red cells in some aplastic anemia patients may develop abnormalities similar to those seen in paroxysmal nocturnal hemoglobinuria[4]. For this reason it is worthwhile screening all patients diagnosed as having aplastic anemia by performing an acid serum hemolysis test.[5]

In general, lymphadenopathy or hepatosplenomegaly are absent at the onset of the disease, but may develop later. The administration of multiple blood transfusions with chronic reticuloendothelial stimulation is thought to account for this. The presence of visceromegaly or lymphadenopathy in a patient presenting initially as a pancytopenia should always alert the physician to the possibility of an underlying process such as leukemia or lymphoma.

Case History: A.S. a 64 year old school teacher was referred to Yale New Have Hospital because of the development of a pancytopenia while receiving indomethacin for arthralgias. She had never received blood transfusions. Physical examination revealed pallor, scattered ecchymoses and a palpable splenic tip. There was no palpable adenopathy. Chest X-ray, IVP and gastrointestinal X-rays were normal or negative. A prominent splenic shadow was reported on the IVP scout film. Marrow trephine revealed a hypoplastic marrow with no abnormal cells seen. A hemogram revealed a moderately severe pancytopenia; liver function studies, uric acid, and Coombs Test were normal or negative. The patient was therefore considered to have a drug induced aplastic anemia and was treated with corticosteroids. There was a gradual improvement in the pancytopenia, and she was discharged to be followed by her private physician. Approximately two months after hospital discharge she was noted to have developed generalized lymphadenopathy. A lymph node biospy revealed lymphosarcoma.

The prognosis in patients with "aplastic anemia" is poor but not as poor as was formerly supposed. Some patients after a period of two to three years may develop a frank acute leukemia. The concept

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This project was supported by Public Health Service Grant CA 08287-02

DR. PASQUALE EMIL PERILLIE, Assistant Professor of Medicine, Yale University School of Medicine. Recipient of U.S.P.H. Career Development Award.

of pre-leukemia has developed from the observation of such patients. A small percentage of patients may undergo a spontaneous remission[6]. About 25 per cent of patients will attain a partial or complete remission in response to therapy[7]. The clinical experience of some authors has suggested that those patients with anemia alone or those with hypercellular marrows have a better prognosis in terms of overall survival[6]. Our experience has been consistent with this observation.

In the general treatment of such patients one should determine as accurately as possible whether the patient has been exposed to drugs or chemicals known to have the potential to produce depression of hematopoietic function. If such a history is obtained an important part of the therapy is removal of the patient from and avoidance of further exposure to the known toxin. The prognosis in patients with a good history of exposure to toxins is better than those who develop their disease "spontaneously" [2].

Specific treatment of this group of disorders has been unsatisfactory. Although appropriately attempted in most patients, treatment with the usual hemantics such as iron, folic acid, vitamin B_{12} or pyridoxine have usually been of no avail. The mainstays of treatment in these patients are blood transfusions, coriticosteroids, androgens and splenectomy.

Transfusions should be kept to a minimum and are given to keep the patient symptomatically comfortable. It is important to avoid unnecessary transfusions in order to minimize the increased risk such patients have to developing hepatitis, iron-overload and sensitization to red cells, white cells or platelets.

Corticosteroids usually in the form of prednisone are administered in dosages of 40-60 mg per day. Although perhaps less than 15 per cent of such patients will respond to corticosteroids, experience has shown that beneficial response may occur after as long a period as three months of therapy. In patients who relapse when corticosteroids are withdrawn we have attempted long term corticosteroid therapy by administering steroids twice weekly at dosages which are equivalent to one half the total amount the patient required weekly when the drugs were given daily. In this manner we have at times been successful in maintaining a satisfactory response and in partially offsetting some of the undesirable effects of long term corticosteroid therapy.

A variety of anabolic or androgenic agents have been used in the treatment of this disorder. Until recently we have noted no significant difference in the response to the general agents available. Amongst the agents tried had been testosterone proprionate, testosterone enanthate and fluoxymesterone. More recently, on the basis of the enthusiastic report of Sanchez-Medal, et al, we have begun using oxymetholone[8]. The daily dosage employed has been between 60 to 80 mg. With these dosages, significant fluid retention may develop so that restriction of salt intake is important. Our initial experience with this preparation has been fair but appears to be better than with the anabolic agents previously employed. As with corticosteroids, these drugs should be given a minimum trial of three months before deciding upon their effectiveness.

The role of splenectomy in the treatment of "aplastic anemia" continues to be controversial. Since there is no reliable method for selecting patients for splenectomy we have reserved splenectomy for specific situations. Splenectomy is attempted in patients who have had an adequate trial of all available forms of therapy and whose transfusion requirements have become inordinately large. In such patients one also frequently finds that the massive transfusion requirement is associated with the development of sensitization to a variety of subgroups of red cells. This usually presents a significant problem in obtaining adequate amounts of type specific blood for transfusion. In this situation the cellularity of the marrow or the presence or absence of splenomegaly are not decisive factors in attempting splenectomy. We and others have had patients with hypocellular marrow and absence of clinical or laboratory evidence of splenic hyperfunction benefit by splenectomy.

Case History: J.D., a 63 year old retired male factory-worker, had been treated for one year for an unexplained pancytopenia associated with a moderately hypocellular bone marrow. There was no history of exposure to drugs or other toxins. Treatment had consisted of the administration of parenteral B_{12}, folic acid, pyridoxine, corticosteroids and androgens. The patient continued to require 4 units of packed red blood cells every 10-14 days to maintain his hematocrit at approximately 25 per cent. His course in addition, had become complicated by the development of pyrogenic reactions to transfusions thought to be due to the development of leukoagglutinins. In evaluating the patient for possible splenectomy a Cr^{51} red cell survival and spleen, liver ratio revealed a slight reduction in red cell survival (21 days—normal 28-32 days) and a normal spleen to liver ratio (2:1). Despite this, because of his progressively greater transfusion requirements, splenectomey was performed.

Since splenectomy he has required 2 to 3 units of whole blood every 8 to 12 weeks to maintain his hematocrit at 30 to 35 per cent.

The major clinical complications in "aplastic anemia" patients are bleeding and infections. Bleeding is usually due to thrombopenia and can be temporarily controlled by the use of fresh whole blood, platelet rich plasma and platelet concentrates. When infection is present, appropriate antibiotics are used when the causative organism has been identified. In the presence of signs and symptoms of infection and inability to isolate a pathogenic organism we have used a selected number of antibiotics in rotational sequence as described in another part of this symposium by Fink and Kaplan.

It is apparent, in light of the variability in course, manifestations and responsiveness to treatment that many diseases of different etiologies and biochemical abnormalities have been probably unwittingly lumped together under the broad designation of "aplastic anemia". It can be anticipated with continued study of such patients that more precise designations as to etiology and treatment will be forthcoming.

Generic and Trade Names of Drugs

Indomethacin—*Indocin*
Testosterone enanthate—*Delatestryl*
Fluoxymesterone—*Halotestin*
Oxymethalone—*Adroyd*

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On Being A Patient

You cannot be a perfect doctor, till you have been a patient. You cannot be a perfect surgeon, till you have enjoyed in your own person some surgical experience. Enjoyed, I say, and stick to the word. Count the ways of enjoyment. To be the dear object of so much care and friendship, to be compassed about with hopes and prayers, is there no pleasure in that? To behave nicely, and nothing common do or mean, upon that memorable scene, but lie on the operating-table like Patience on a monument, is there no pleasure in that act of self-control?—Stephen Paget (1855-1926)

DRUG INDUCED AGRANULOCYTOSIS

Sandra S. Kaplan, M.D. & Martin E. Fink, M.D.

Agranulocytosis is the most common drug induced blood dyscrasia[1] and carries a mortality of 20% to 30% even with optimal management[2]. It was first presented as a separate clinical entity in 1922 by Werner Schultz[3] who described it as a syndrome characterized by severe sore throat, sudden drop in the circulating granulocytes, prostration, sepsis and death.

The numbers and types of drugs giving rise to agranulocytosis is extremely large and is steadily increasing as new drugs are developed. These drugs may be divided roughly into two types: (1.) agents which will always suppress granulopoiesis if given in sufficient quantity such as alkylating agents, antimetabolites and benzol: and (2.) agents which occasionally produce leukopenia in susceptible persons on a hypersensitivity basis without relationship to dose administered. The major categories of drugs in the latter group are analgesics (especially amidopyrine and phenylbutazone), antithyroid drugs, anticonvulsants, sulfanilamides, antihistamines, antimicrobial agents, tranquilizers (especially chlorpromazine), and oral antidiabetic agents.

There are at least two major types of idiosyncratic hypersensitivity drug induced granulocytopenias. The first type is exemplified by amidopyrine[4] and may occur after only a short period of medication. It often begins quite suddenly with a chill, followed by rapid disappearance of granulocytes from the peripheral blood. There is then a short latent period with some malaise, not infrequently followed in 12-24 hours by a necrotic sore throat without pus, high fever and prostration. At any time during the granulocytopenic phase which may last from a few hours to many days, the affected person may develop multiple focal infections or overwhelming septicemia. The initial chill is thought to be due to rapid destruction of granulocytes by an immune mechanism rather than a manifestation of infection. Regional lymphadenopathy may occur but splenomegaly, bone tenderness and generalized lymphadenopathy are rare. It occurs about three times as often in women as in men, and usually occurs past the age of 40[5]. The blood count reveals a severe leukopenia with total granulocyte counts often as low as 0-200/mm[3]. The bone marrow characteristically shows normal megakaryocytes and red cell precursors, and in severe cases examined early, granulocytes may be completely absent[6]. Often one sees a striking lack of myelocytes, metamyelocytes and more mature granulocytes[7]. Circulating leukocyte antibodies frequently are found in this type of agranulocytosis. In a classical study by Moeschlin and Wagner[8], it was shown that blood taken from a sensitive patient three hours after a test dose of amidopyrine and transfused into normal subjects, produced a severe granulocytopenia in the recipient within 30 minutes, which persisted for several hours. Also, administration of only a fraction of the usual dose of this drug to a patient known to be sensitive produces striking granulocytopenia in one to three hours which persists for several days.

The second major type of idiosyncratic hypersensitivity drug induced agranulocytosis is exemplified by the phenothiazines[9]. Characteristically it begins after a longer period of continuous or intermittent treatment, and does not have the type of explosive onset seen in the first category. In this condition the white blood count may fall slowly at first and the leukopenia may in fact be found only on routine examination. However, once it begins to fall, it reaches a low point in two to five days and may reach the very low levels seen with amidopyrine. The clinical picture and the bone marrow at this point are identical with that outlined for amidopyrine. The age incidence in this type of agranulocytosis is similar to the first type but the sex difference is more pronounced, women being affected four to six times more commonly than men. Leukocyte antibodies in agranulocytosis due to phenothiazines have not been found. However, Pisciotta has found[10] that chlorpromazine inhibits DNA synthesis resulting in a prolongation of generation time and reduction of cell division. Persons known to be sensitive to chlorpromazine, unlike normal persons, were found to have a lim-

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ited proliferation potential and thus were unable to overcome the toxic effect of chlorpromazine resulting in decompensation of marrow function.

The incidence of agranulocytosis differs for each offending agent. At present, the phenothizanes are quantitatively the most important cause due to their wide usage. Chlorpromazine has an estimated incidence of 0.13-0.7 per cent. However, the antithyroid drugs account for a larger number of cases in proportion to their use with an incidence of 0.45 to 1.75 per cent. Amidopyrine also has a high incidence at 0.86 per cent, but it is not used very extensively now. A complete listing of drugs causing agranulocytosis along with frequency of occurrence can be found in the Reporting on Blood Dyscrasias[1].

The establishment of a diagnosis of drug induced agranulocytosis depends upon the history of exposure to an offending drug along with the rather typical sudden onset and rapid recovery. The only certain proof, however, is the demonstration of recurrence following readministration of the drug once recovery has occurred[5, 6]. The hazards associated with this procedure, however, preclude its practical clinical application. An attempt to demonstrate drug dependent antibodies in the serum of the affected individuals should also be made. However, failure to demonstrate antibodies does not rule out the causal relationship of the drug to agranulocytosis[11]. Also, the finding of antibodies does not necessarily establish this causal relationship,[12] since persons who have received blood transfusions, and women who have had one or more pregnancies may have leukoagglutinins in their serum. These antibodies, however, will probably react both in the presence and absence of drug from the mixture, while drug dependent antibodies would agglutinate leukocytes only in the presence of the drug being investigated[2, 13].

Treatment of Acute Agranulocytosis

The identification of any offending agent, either drugs, chemicals or exposure to ionizing radiation assumes the highest priority in the management of acute agranulocytosis since immediate removal of the offending agent and the prohibition of its further use is mandatory.

The development of severe infection in the presence of granulocytopenia then becomes the chief concern of the clinician faced with the care of this condition. The risk that an infection will ensue becomes critical once absolute granulocyte counts become depressed below levels of 500/mm.[3] and the incidence rises sharply as granulocyte counts decrease below this level[14]. Meticulous care to prevent skin breaks (bed sores or ulcers) as well as maintenance of mouth hygiene is important.

Critical data on the use of prophylactic antibiotics is lacking. Rotational schemes of treating patients with a series of three to four different antibiotics (each of which is used for three to five days in turn and then is repeated in the same sequence) have been attempted with the hope of suppressing intercurrent infections as well as preventing the emergence of resistant organisms.

At the present time it would appear that the most judicious course is one of watchful waiting for evidence of infection—fever, sore throat, headache with stiff neck, cough, dysuria, or appearance of a rash. Infections seen most commonly in this disease are pharyngitis, pyelonephritis and septicemia. Organisms most commonly found are E. coli, M. Pyogenes var. aureus (coagulase positive), and Ps. aeurginosa[15]. Pseudomonas infections are the most difficult to treat because of their resistance to most antibiotics. It is important to emphasize that the absence of physical findings in the presence of fever in a leukopenic patient does not exclude infection. It is well to remember that fungal infections may occur in agranulocytosis and these organisms should be looked for, using suitable culture techniques. Candida is the most common fungus encountered, and can be controlled with Mycostatin. If intestinal overgrowth becomes a problem, a solution of 0.1% amphotericin may be used. Occasionally organisms which are not usually considered pathogenic (e.g. M. Pyogens, var. albus, coagulase negative) will produce septicemia.

The prompt culturing of blood, urine, sputum, nasapharynx, and even spinal fluid should be carried out with the appearance of fever or presentation of localizing signs. After a series of two or three blood cultures have been obtained, at one to two hours intervals, administration of antibiotics to patients with sudden fever should not be delayed. Resistance to infection often is so poor that a patient may die before the organisms are identified. In the absence of any clear source of infection, kanamycin sulphate and sodium colistimethate parenterally will provide a good spectrum of coverage in particular against gram negative organisms. The additional use initially of one of the synthetic penicillins, such as methicillin or sodium nafcillin, will provide excellent coverage against penicillinase producing staphyloccoccus aureus.

The role of corticosteroids and/or androgens in the recovery from acute agranulocytosis is uncertain primarily because it is unclear as to whether or not the patient would have recovered without the use of these hormones. Pisciotta et al have been unable to show any clear differences in the clinical courses of treated and untreated patients[9]. Unless the patient shows no improvement and absolute granulocyte counts remain critically low within seven to ten days of the onset of the granulocytopenia, steroid therapy should be withheld since it may only serve to increase the risk of supervening infection. The only clear indication for the use of corticosteroid therapy in acute agranulocytosis is with the development of gram negative septicemia accompianed by shock. As soon as the infection is under control and blood pressure levels have stabilized, every attempt should be made to withdraw steroid therapy gradually.

Leukocyte transfusions are not currently available to most clinical facitities; however, they may be helpful in those patients whose disease is quite obviously acute and in whom there is hope that the granulocytopenic state is only transitory. Techniques of white cell transfusion are currently being developed at the National Cancer Institute[16]. Current techniques utilize granulocytes from donors with chronic granulocytic leukemia. In spite of the fact that only 5 per cent of the transfused cells remain in the vascular compartment and have a half life in the circulation of only one day, these transfusions have procured lysis of fever and apparent cure of septicemia. Blood transfusion itself is not indicated unless severe anemia is present and this is observed only rarely. Gamma globulin administration is not indicated since these patients do not exhibit deficiency of immune globulin synthesis.

Considerable efforts have been exerted in most hospitals to effect complete isolation of the patient with acute granulocytopenia by the technique of reverse precautions. Patient isolator systems are being developed by the National Cancer Institute for patients undergoing drastic chemotherapy in an attempt to provide prophylactic reduction of resident-body pathogens[17]. Such techniques might well have future application in the management of patients with acute severe granulocytopenia, to tide them over the transitory period of high-risk susceptibility to infection. In our experience, conventional isolation techniques cause unnecessary labor to the nursing staff and serve only to discourage good nursing supervision, which in itself may be a critical factor in the outcome of the illness. Seeing all of his medical attendants administer to him in gowns, caps and masks, serves only to increase the patient's apprehension.

Those patients who do not die promptly of infection may be expected to begin showing improvement 5-10 days after cessation of the offending drug. The recovery phase of drug induced agranulocytosis is usually heralded by the appearance in the peripheral blood of immature granulocyte precursors such as myelocytes, metamyelocytes, and occasionally myeloblasts. The leukocytic reaction may be quite rapid and marked degrees of leukocytosis may occur. There is some evidence that the initial phase of bone marrow recovery is characterized by ineffectual leukopoiesis, and that recovery may therefore be predicted by a rise in serum muramidase before granulocytic cells appear in the peripheral blood[18].

Prior to the availability of antibiotics the mortality in drug induced agranulocytosis was 80-90 per cent[5]. Although the outlook is considerably improved, the present mortality of 20-30% continues to necessitate a guarded prognosis especially where advanced age and general debility are present.

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Imperturbability

Imperturbability means coolness and presence of mind under all circumstances, calmness amid storm, clearness of judgment in moments of great peril, immobility, impassiveness, or, to use an old and expressive word, *phlegm.* It is the quality which is most appreciated by the laity though often misunderstood by them; and the physician who has the misfortune to be without it, who betrays indecision and worry and who shows that he is flustered and flurried in ordinary emergencies, loses rapidly the confidence of his patients. . . .

In a true and perfect form, imperturbability is indissolubly associated with wide experience and an intimate knowledge of the varied aspects of disease. With such advantages he is so equipped that no eventuality can disturb the mental equilibrium of the physician; the possibilities are always manifest, and the course of action clear. From its very nature this precious quality is liable to be misinterpreted, and the general accusation of hardness, so often brought against the profession, has here its foundation. Now a certain measure of insensibility is not only an advantage, but a positive necessity in the exercise of a calm judgment, and in carrying out delicate operations. Keen sensibility is doubtless a virtue of high order, when it does not interfere with steadiness of hand or coolness of nerve; but for the practitioner in his working-day world, a callousness which only thinks of the good to be effected, and goes ahead regardless of smaller considerations, is the preferable quality.—OSLER (*Aequanimitas,* 1889). *The Quiet Art: A Doctor's Anthology.* Compiled by DR. ROBERT COOPE. Edinburgh & London, E. & S. Livingstone Ltd., 1952, p. 205.

DELAYED COMPLICATIONS OF TRANSFUSION

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Coincident with the increasing use of blood transfusions there has developed an increased awareness of their complications. Physicians are rightly concerned about the consequences of mismatched blood or improper identification of recipients, since such errors are immediately followed by serious transfusion reactions. The dramatic nature of such catastrophic events tends to overshadow the equally important problems of delayed complications. Dangerous and even fatal sequelae may develop as late as six months after transfusion. These delayed complications loom even more serious since not infrequently they strike a patient who has regained his health and in whom the original illness is cured. In this paper those complications developing two or more days after transfusion will be discussed under two major headings: 1) the transmission of disease and 2) hazards of isoimmunization.

TRANSMISSION OF DISEASE

Syphilis: Although rarely seen today the transmission of syphilis is a well-known complication of blood transfusion. The organism, *T. pallidum*, can be found after the primary infection and circulates for about four weeks before the first serologic evidence of syphilis is manifest[1]. Should an infected person donate blood during this time he may transmit syphilis even though he has a negative serologic test for syphilis. The spread of syphilis by transfusion is very infrequent, however, because of two important considerations. In all but the most urgent situations a serologic test for syphilis is done on all blood donors before their blood is used for transfusion. This is done, in Connecticut, at the Blood Center in Hartford. Over the past six years the frequency of positive tests has been constant at 0.03 per cent[2]. While many of these represent biologic false positive reactions, and not syphilis, all blood from seropositive donors is discarded. Thus, only donors who are in the first stages of infection with a negative serology are potentially dangerous. In addition, the *T. pallidum* does not survive longer than 96 hours in citrated blood stored at 4°C [3]. Bank blood that is more than three days old can not transmit the disease. For these two reasons syphilis is rarely seen as a delayed complication of blood transfusion.

The physician can take additional comfort from the knowledge that effective treatment is available for syphilis. A recipient who receives blood from an infected donor should have adequate treatment at once along with careful serologic evaluation, including a serologic test for syphilis, six months after transfusion.

Serum Hepatitis: The transmission of viral hepatitis is the major problem in blood transfusion today. The incidence of post-transfusion *icteric* hepatitis ranges from 0.2 to 4.1 per cent of recipients of whole blood or packed red cells[4]. These data are even more alarming when related to the fatality rate of at least 10 per cent in such cases. Recent studies[5] suggest that the incidence of non-icteric hepatitis is higher, perhaps as high as 8.7 per cent of patients.

The incidence of post-transfusion hepatitis is, in all probability, related to the donor population. In particular, the use of "commercial blood" seems to be associated with an increase in the attack rate of serum hepatitis. In one study[6] there was a four-fold increase in the incidence of hepatitis when blood was purchased from a particular commercial source. Other studies[7,8] are in agreement with this conclusion, although one contrary report[9] has been published. The experience in Connecticut is difficult to judge since there has been no concerted effort to search out cases of post-transfusion hepatitis. As a result, the data are misleading and indicate only the lowest possible incidence of the disease. In the six year period, 1960 to 1966, 574,587 units of whole blood were used by the hospitals in this state. During that period only 116 cases of serum hepatitis were reported to the Connecticut Blood Center[2]. If it is assumed that the usage was about 3.0 units per patient almost 200,000 patients were transfused giving an incidence of hepatitis of at least 0.058 per cent of patients. This is an extremely low number and suggests, even in the face of poor reporting, that the donor population in Connecticut has a low carrier rate for the hepatitis virus.

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The importance of a "safe" donor population cannot be overemphasized since there is, as yet, no satisfactory test to identify those apparently healthy donors who are carriers of the hepatitis virus. Needless to say, there have been many attempts at laboratory evaluation of blood donors to eliminate those who are hepatitis carriers. For the most part these studies have been done using liver function tests as screening methods. Some reports have been encouraging, but no test or battery of tests has been adopted. Bang et. al.[10] reported in 1959 that the incidence of hepatitis was 1.5 per cent when donors had a normal serum glutamic oxalacetic acid transaminase (SGO-T) value as compared with 3.5 to 5.5 per cent when the SGO-T level was elevated. In addition, they showed that the higher the value for SGO-T the higher the incidence of hepatitis. Despite this report neither the American Red Cross, the American Association of Blood Banks nor even the hospital in which Bang's study was done recommends or uses this test as a donor screening method. In a like manner, the incidence of post-transfusion hepatitis has shown a "significant reduction" when a battery of liver function tests was used to screen prospective donors[11]. Another author[12] reported in 1963 that "the use of thymal turbidity and flocculation tests appears to be valuable" and still another[13] that there is "a 16 to 1 chance that a donor who might be a carrier could be found among those with an abnormally prolonged activated partial thromboplastin time."

These and other similar observations have not been challenged: nor have they led to the use of any tests to detect hepatitis carriers among prospective blood donors. This seeming paradox is best explained by a combination of facts. The data are suggestive, not definitive. Because of the low incidence of the disease and the importance of meticulous follow-up adequate studies are hard to do. The routine use of the liver function studies would add to the expense of blood transfusion. But, perhaps, most important is the potential loss of large numbers of "safe" donors. The use of liver function tests to eliminate hepatitis carriers would eliminate so many uninfected donors that the universal blood shortage would become even more critical. Till definitive data are available blood banks can not suffer this loss. In all probability the cure, on a national level, would be worse than the disease. Hence, donor screening for hepatitis carriers awaits a more specific and reliable test.

Modification of Post-Transfusion Hepatitis The recent report of Merick, Ward and McCollum[14] has stimulated new interest in the use of gamma globulin injections to suppress post-transfusion hepatitis. These authors evaluated the use of gamma globulin injections in 774 patients who received 3,618 blood transfusions. The patients were divided into one control and three treatment groups. Patients in the treated groups were given gamma globulin in doses of 20 or 30 ml on different dosage schedules, including treatment before and for up to one month after transfusion. The incidence of icteric hepatitis was 9.2 per 1000 units of blood in the untreated group as compared with 3.2 per 1000 units of blood in the treated groups. Of interest was the almost identical incidence of anicteric hepatitis in both groups; 13.3 per 1000 units for the control group and 12.8 per 1000 units for those who were treated with gamma globulin. These authors concluded that "10 ml of gamma globulin in the week after blood transfusion and again one month later will prevent about 3/4 of the cases of icteric post-transfusion hepatitis." Although these data are encouraging there is still insufficient evidence to recommend the widespread use of gamma globulin; nor would such a recommendation be practical. It has been stated[15] that the amount of gamma globulin needed to implement such a policy would be about three times the total present annual supply and 50 per cent above the maximum industrial production capacity of the nation[16]. Furthermore, there is no evidence that the icteric variety (the only kind prevented by gamma globulin in the Merick study) is any more dangerous than the non-icteric type of disease. At present it seems wise to limit the use of gamma globulin to those patients who are in a particularly "high risk" group. This surely includes any patients who have been given fibrinogen where the risk of hepatitis may be as high as 25 per cent per unit.

Other Diseases: It seems reasonable to conclude that almost any infectious disease could be transmitted by transfusion. The incidence of such unfavorable events is, however, quite low. Brucellosis, toxoplasmosis and malaria have been reported, but of these only malaria is a significant problem. The parasites of malaria are hardy and remain viable in stored blood for at least 14 days. In addition, suppressive therapy for malaria makes it possible for a blood donor to be infective though asymptomatic. It is wise to wait for at least two years after a person has received suppressive therapy or has been in a malarious area before accepting him as a blood donor. Persons who have had more than one attack of malaria should be rejected permanently.

ISOIMMUNIZATION

At least 120 different blood groups (factors) have been described. All are capable of acting as antigens and can, at times, stimulate a recipient to produce a potent blood group antibody. Because of the large number of blood group antigens it is absolutely impossible to provide any recipient with blood that exactly "matches" his own. It is essential to use blood that is ABO compatible and, in all but unusual situations, to use Rh negative blood for Rh negative recipients. Any attempt to match other factors, such as Kell or hr' (c), is unnecessary and not required. This is because the amount of additional typing that can be done will be inadequate to influence the incidence of isoimmunization. In a careful study of blood recipients at the Yale-New Haven Hospital Dowaliby[17] found this incidence to be about 3 per cent. Isoimmunization as a delayed complication is usually of little consequence. Although these newly formed isoantibodies will not react with or destroy the recipients own cells, all future transfusions must, of course, be compatible, not only as regards ABO and Rh but also with respect to the new isoantibody. If the antibody is directed against a low frequency antigen (such as Kell) there will be little difficulty in finding compatible blood. On the other hand, should the antibody be specific for a high frequency antigen it will be difficult or, at times, almost impossible to find a compatible donor. In such situations the delayed complication of isoimmunization becomes a major medical problem, and it may be necessary to use the rare donor files maintained by the American Association of Blood Banks or the National Blood Program of the American Red Cross to locate donors of the right type. Consultation with large blood centers such as the Connecticut Red Cross Center in Hartford will aid in locating such donors.

Incompatible Crossmatches: Isoantibodies formed as a *primary* response to transfusion usually do not appear till at least two weeks after the first immunizing transfusion. They may, at that time, slowly hemolyze the now incompatible donor cells. This does not result in an acute hemolytic episode and is usually recognized only by the gradual onset of slight anemia. There are no clinical symptoms of transfusion reaction, no hemoglobinuria, no hemoglobinemia, and jaundice is usually absent or very minimal. Nearly always, blood group antibodies, once formed, persist for long periods of time (18, 19) and can be demonstrated when an indirect antiglobulin test is done. In addition, a proper crossmatch will detect them before transfusion and allow the choice of compatible blood.

Delayed Hemolytic Reactions: As described above, most blood group antibodies, once formed, can be found in the serum of the patients almost indefinitely. A good crossmatching test detects them and allows the selection of compatible blood. If this is not done an acute hemolytic reaction will invariably occur at the time of transfusion.

Unfortunately, some blood group antibodies, particularly those in the Kidd and Duffy systems, do not always follow this pattern of long persistence. These antibodies in particular, but others as well, may disappear from the circulation in a relatively short time. Thus the patient has a negative indirect antiglobulin test and there is no difficulty with crossmatching. *The antibody producing cells, however, are sensitized to the antigen in question and transfusion of "apparently" compatible blood initiates a secondary response.* As in all such anamnestic responses, immunologic memory leads to rapid production of large amounts of antibody when the antigen in question (blood in this case) is infused. There is then a delayed hemolytic reaction, usually about six days after the apparently compatible transfusion has been given. The following case report indicates that such reactions can be serious.

The patient was a 32 year old male who had had many previous hospital admissions and transfusions. At the age of 19 gastrointestinal bleeding was treated with the first of his many blood transfusions. A diagnosis of esophageal varices, extrahepatic portal obstruction and splenomegaly was made. Repeated episodes of hemorrhage were treated by transfusion of whole blood. At age 24 surgery was done for the transesophageal ligation of bleeding varices. Two weeks later splenectomy and spleno-renal anastomosis was done. Several admissions, each for gastrointestinal bleeding, followed. Transfusions on each of these were without incident. On his sixth admission the indirect antiglobulin (Coombs) test was found to be positive and anti-Kell was identified in his serum. Because of continuing episodes of gastrointestinal hemorrhage it was decided to repair a hiatus hernia. At operation 10 units of Kell negative *compatible* blood were given without evidence of transfusion reaction. His hematocrit value on the day after operation was 42 per cent and his bilirubin value 1.44 mg per cent. The hematocrit value remained above 40 per cent for the first six postoperative days. On day seven he had chills and fever, an abrupt fall in hematocrit to 25 per cent and free hemoglobin in the plasma and urine. Serum haptoglobin was zero. The direct as well as the indirect antiglobulin tests were now strongly positive and two additional antibodies, anti-Duffy (anti-Fy^b) and anti-Kidd (anti-Jk^a) were found in his serum along with the anti-Kell. Only two units of Kell negative, Duffy negative, Kidd negative blood could be obtained from the frozen blood bank of rare donor bloods.* These were given without clinical reaction. Despite this, renal shutdown and severe anemia progressed. No compatible blood could be found although centers for rare donors in New York, Washington, Chicago, Milwaukee and Boston were consulted. He died eight days after the delayed hemolytic reaction.

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*Supplied through the courtesy of Dr. Charles Huggins, Mass. General Hospital, Boston, Mass.

While this case is somewhat unique, particularly because of the severity of the reaction, it is likely that the less severe delayed hemolytic reactions are more common than has been appreciated. It is essential that these be considered in the diagnosis of unexplained anemia, jaundice or obscure findings in the week after transfusion. Proper evaluation includes a direct and indirect antiglobulin test. If either of these are positive attempts to identify the antibody involved are indicated so that future transfusion, if needed, will be of truly compatible blood.

The risk of transfusion complications does not end when the blood has finished running. Delayed reactions and transmitted disease, such as hepatitis, remain to haunt the physician and his patient long after the actual day of transfusion.

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GENERALIZED BLEEDING ASSOCIATED WITH DIFFUSE INTRAVASCULAR COAGULATION*

Yale Nemerson, M.D.

Introduction

The apparent paradox of generalized and frequently massive bleeding being associated with diffuse intravascular clotting can be explained by the fact that blood coagulation results in the destruction of several clotting factors and the blood platelets. The deleterious effects of intravascular coagulation may be the result of thrombi or the direct result of severe hemorrhage. The consequences of the latter are self-evident while the consequences of multiple small emboli and thrombi may be occult. In this paper I shall discuss the hemorrhagic complications of intravascular coagulation because it is the depletion of the clotting factors that leads to the diagnosis and to the therapy of this condition. To do so, I shall divide this discussion into several parts: 1) the mechanisms of blood coagulation, 2) pathogenesis of intravascular coagulation or "defibrination" and 3) clinical manifestations and therapy.

Mechanism of Blood Coagulation

Blood coagulation is best conceived of as a series of reactions in which several proenzymes are converted to enzymes in a sequential manner. The overall scheme is illustrated in Figure 1. Many of the steps have been well defined, but information about several is still sketchy. Suffice it to say that the order of the reactions is probably correct although some may not be of the type alluded to above; i.e., conversion of a proenzyme to an enzyme.

It is important to understand that there are no active enzymes of the coagulation system found in the circulating blood[1]. This implies that blood coagulation is not a continuous process, but must be initiated by some activating agent not normally associated with the circulation. Under physiological circumstances this is thought to be contact with injured blood vessels. It is felt by many that the same process is involved in pathological conditions such as thrombosis. That is, the primary event in both normal hemostasis and abnormal thrombosis is damage to a blood vessel.

The biochemical mechanism by which blood coagulation is initiated is not understood. Recently, evidence has been adduced that collagen, a constituant of vessels, activates Hageman factor (factor XII)[2]. On the other hand, if this were the sole or even an important mechanism, one might expect patients with a deficiency of this factor to have a severe hemorrhagic diathesis. It is well known, of course, that patients with this deficit have few symptoms. Moreover, the concentration of collagen needed to activate Hageman factor *in vitro* appears to be in excess of what might be available in the blood vessels.

Another way in which the coagulation mechanism can be activated is via the so called tissue factor or extrinsic pathway. It has been shown that extracts of certain tissues activate coagulation through a specific interaction with factor VII[3,4]. The product of this reaction enzymatically activates factor X, thus bypassing the reactions involving factors XII, XI, IX and VIII. This is readily accomplished in the test tube by adding tissue extracts and calcium ions to plasma. Under standard conditions this is the well-known "one stage" or Quick prothrombin time. It should be kept in mind that this is somewhat of a misnomer as the tissue factor pathway of blood coagulation involves five clotting factors (Figure 1).

Thus there are two ways by which blood coagulation is known to proceed: 1) via the "intrinsic" pathway, involving all known factors but factor VII, and 2) by way of the tissue factor mechanism. The relative importance of each of these is not known, but it is likely that the former is more important in as much as a deficit in the intrinsic system is clinically more serious than one in the extrinsic system.

When blood is clotted in the test tube, certain of the factors are destroyed. The most labile in this regard are factors VIII (antihemophiliac fac-

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The experimental work referred to was supported by a grant from the USPHS (HE-09057).

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tor), factor V (labile factor), prothrombin and fibrinogen. The blood platelets, although not strictly speaking a clotting factor, are also destroyed during the course of coagulation. Therefore, one can define in biochemical terms the difference between plasma and serum: with respect to plasma, serum is deficient in factors VIII, V, prothrombin, fibrinogen and platelets.

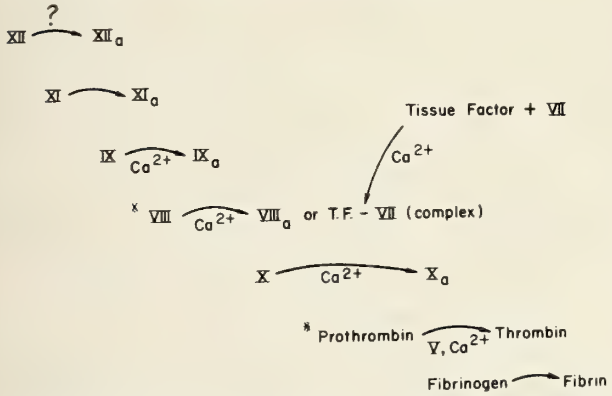

Figure 1: Schematic representation of the mechanism of blood coagulation. The reactions on the left are those involved in spontaneous or "intrinsic" coagulation, and those on the right, initiated by the addition of tissue extracts, are of the "extrinsic system." Common synonyms for some of the factors are: XII, Hageman factor; XI, plasma thromboplastin antecedant, PTA; IX, plasma thromboplastin component, PTC; VIII anti-hemophilic factor; X, Stuart-Prower factor; VII, SPCA; V. labile factor. The reactions indicated with an asterisk require phospholipid.

In patients in whom diffuse, generalized clotting has occurred, the circulating blood can be viewed as a mixture of plasma and serum. That is, there is a decrease, but not an absence, of the factors that are destroyed during coagulation. Thus, a complex hemostatic defect arises which is reflected in abnormalities of *all* the common tests of blood coagulation. Conversely, normal findings in these tests usually rule out diffuse intravascular coagulation. The tests used for such screening in this hospital are the prothrombin time and the partial thromboplastin time (PTT). The latter is essentially a plasma clotting time which has been treated in a fashion to optimize glass contact and phospholipid content. It has the virtues of being rapid, reproducible and extremely sensitive. Short of specific factor assays which must be performed for the definitive diagnosis of intravascular coagulation, the PTT is the most useful single test available for evaluating the integrity of the coagulation mechanism.

Intravascular coagulation must be differentiated from primary fibrinolysis because the therapy of each differs (see below), and is probably contraindicated in the other. The incidence of fibrinolysis appears to be quite rare with respect to intravascular coagulation, which is fortunate as the biochemical findings in fibrinolysis may resemble those of intravascular coagulation: decrease in factor VIII, V, and fibringen. Of help is that the platelets tend to be preserved in fibrinolysis, and prothrombin depressed only slightly. The latter is not much help in the differential diagnosis as prothrombin is usually not markedly reduced in intravascular coagulation.

The most significant findings in fibrinolysis are abnormalities in tests in which the actual lysis of fibrin is measured. This may be done in the euglobulin technique in which the lysis of the patient's own fibrin is evaluated after first precipitating both clotting and lytic factors at low ionic strength and pH; by a plasma clot lysis test, in which the patient's plasma is clotted with calcium and observed; or by a variety of tests in which the patient's plasma is tested against exogenous fibrin. In the overwhelming majority of cases of diffuse intravascular coagulation these tests are normal or are at most barely abnormal[5]. On the other hand, if extremely sensitive tests of fibrinolysis are employed such as the tanned sheep cell hemagglutination inhibition assay developed by Merskey et. al. abnormal results are obtained in all cases of intravascular coagulation[6]. This indicates that there is some element of fibrinolysis operative in intravascular coagulation, but it is most probably of no pathological significance, and may even be protective against the deleterious effects of the small fibrin emboli thought to be formed in this condition.

Pathogenesis of the Defibrination Syndrome

There are two ways to experimentally defibrinate animals which may have relevance to human disease: by infusing thromboplastic substances such as tissue extracts or thrombin, and by the properly spaced injection of bacterial endotoxin[7]. The latter is the so called Schwartzman reaction.

Both of these techniques cause a syndrome in animals which resembles the human condition both biochemically and clinically. That is, the animals develop deficiencies in blood platelets and in those factors which are destroyed during coagulation. Moreover, the animals are apt to develop spontaneous bleeding as occurs in the human disease. There are, however, several problems which prevent the uncritical acceptance of either of these models as being relevant to the human state. Firstly, the quantities of tissue thromboplastin that must be infused to defibrinate animals are very large, and one wonders if such amounts are ever available *in vivo*. Moreover, tissue thromboplastins are particulate and should be demonstrable at autospy. Such, however, is usually not the case. The one exception to this may be amniotic fluid embolism which is a complication of pregnancy frequently leading to defibrination. Here, placental particles may be infused into the general circulation. It is these particles and not the amniotic fluid *per se* which are thromboplastic[8], and at autopsy it is not unusual to see debris trapped in the pulmonary circulation[9]. In other conditions which lead to intravascular coagulation, such as gram negative sepsis and disseminated carcinoma, there is no evidence of the release of large quantities of particulate thromboplastins into the circulation.

The injection of very small quantities of bacterial endotoxin at appropriate intervals into rabbits leads to defibrination[10]. This phenomenon, the Schwartzman reaction, can be prevented by pretreating the animals with heparin[11]. If the animals are untreated and the complete reaction allowed to develop, the blood becomes incoaguable due to thrombocytopenia and destruction of several clotting factors. The end result resembles human defibrination in as much as there are similar biochemical findings. It is not unreasonable to suppose that human infection with gram negative organisms leads to similar consequences[12], but it should be emphasized that the Schwartzman reaction is species specific, e.g., rabbits but not rats are susceptible, and there is no direct evidence that humans are amongst the susceptible species.

As we have discussed above, blood coagulation is probably not a continuous process. This means that there are no circulating enzymes but only inert precursors. Therefore, for intravascular coagulation to occur, something must convert a proenzyme into an enzyme. There has been much speculation that phospholipids are responsible for causing intravascular coagulation and experimental models have both confirmed[13] and denied[14] this mechanism. Whether infusions of phospholipid emulsions can lead to defibrination may be settled by further experimentation, but even if it can be demonstrated in experimental animals, again one wonders about the relevance to human disease. In the positive experiments the amount of lipid used was large and in a form which probably never exists in the circulation. The implication of these experiments is that destruction of the natural source of phospholipids involved in coagulation, the platelets, can lead to the release of substances which trigger the clotting mechanism. There are two serious objections to this approach. The first is that phospholipids *in vivo* are associated with protein, that is, they are in the form of lipoproteins and it must be shown that lipoproteins and not lipid emulsions cause defibrination. Secondly, it has never been shown *in vitro* that phospholipid *per se* can convert a proenzyme into an enzyme. That is, there is no evidence that phospholipids can trigger the clotting mechanism by activating a proenzyme[15]. On the other hand, it is certainly true that phospholipids can accelerate blood clotting and in a situation in which the clotting system was activated, the release of phospholipids would be expected to enhance the deleterious effects of intravascular coagulation.

Although it is clear from the above that the basic mechanism of defibrination is not known, it is certainly true that this type of acquired hemorrhagic diathesis frequently presents as a medical emergency. The most frequent causes are complications of pregnancy (placental abruption, amniotic fluid embolism and retained dead fetus) and a variety of neoplasms. There are, however, patients with an assortment of diseases who have developed defibrinating syndromes. Perhaps the most common amongst the latter are severe infections, leukemia (mainly promyelocytic), snake bites and heat stroke. As many of the patients who defibrinate have reversible diseases, it is clearly important to recognize this condition and institute early therapy.

Clinical Conditions and Therapy

Defibrination can take the form of an acute medical emergency characterized by severe, massive bleeding or of a chronic state accompanied by few signs of bleeding or thrombosis. The biochemical findings are also variable, and might relate to the acuteness and severity of the syndrome. The variability of both laboratory tests and clinical states is characterized by these cases from our own experience:

Case 1 (WD): A 67 year old male who had an orchiectomy for carcinoma of the prostate 27 months before his current admission. He had been cared for in a nursing home and was incapacitated as a result of metastatic lesions. He suddenly developed a bleeding syndrome characterized by eccymoses, petechiae and gross bleeding from the urinary tract. He was admitted to the West Haven V. A. Hospital and the laboratory data shown in Table 1 were obtained. Heparin therapy (150 mg per day) was instituted and he was supported with whole blood transfusions. Seven days after therapy was started all the abnormalities of the hemostatic mechanism returned to normal and bleeding ceased. Several weeks after this episode he died as a result of extensive carcinomatosis.

TABLE 1

Patient:	*WD*	*PB*	*RP*
Pro-time	22″	17.0″	17.4″
PTT	——	75″	29.9″
Fibrinogen	128	360	77
Factor V	36%	34%	55%
Factor VIII	22%	92%	153%
Factor X	50%	33%	65%
Platelets	40,000	77,000	145,000
Eug. Lysis	normal	normal	sl. elevated
Thrombin Time	32/20	16/14	22/14

Table 1: The blood coagulation data found at the time of diagnosis of three patients with defibrination. The normal values and abbreviations are: Pro-time (prothrombin time) 12″; PTT (partial thromboplastin time), <45″; fibrinogen, >200 mg/100 ml plasma; Factors V, VIII and X, >60%, platelets, >200,000/mm³; Eug. Lysis (euglobulin lysis time), >90″; Thrombin time, <3″ greater than the control.

Case 2 (PB): A 35 year old woman was admitted for induction of labor at the 40th week of pregnancy. Labor was induced with a Syntocin drip without difficulty. Membranes had ruptured spontaneously 44 hours before the delivery of a still-born child. Her immediate post-partum course was uncomplicated, but 8 hours after delivery a large vaginal hematoma was noted. This was surgically evacuated without undue bleeding. The next morning an episode of hypotension developed which responded to elevation of the foot of the bed. Later that morning she vomited a large quantity of coffee ground material. Laboratory data were obtained and are shown in Table 1. Heparin (250 mg per day) was given along with blood transfusions. Massive bleeding from the GI tract and vagina continued for about 36 hours and then ceased. Heparin was continued for 4 days. By the fifth day, the depressed levels of some of the clotting factors returned to normal. The moderate thrombocytopenia, however, persisted for 10 days, and the platelet count did not rise to normal levels until the 14th day. The patient ultimately was discharged from the hospital in good health.

Case 3 (RP): A 69 year old male consulted his physician because of the sudden onset of easy bruisability. On physical examination he had many ecchymoses covering the lower extremities. Because of his age, he was admitted to the hospital where, in addition to the above, a hard nodular prostate was noted. A complete coagulation work-up was performed and is shown in Table 1. Other data of note was an acid phosphatase of 22 units (normal = under 2.0). Because of his bleeding tendency, biopsy was delayed and estrogen therapy begun. Several days later a biopsy was performed and revealed carcinoma of the prostate. Ten days after admission his fibrinogen had risen to 180 mg/100 ml, bruising had decreased and an orchiectomy was performed. After an uneventful convalescence, he was discharged from the hospital.

These three cases illustrate the spectrum of clinical and laboratory findings encountered in defibrination. The first case exhibited the expected findings and responded well to heparin therapy. The second case had normal levels of fibrinogen and factor VIII, but had thrombocytopenia and a decrease in factors V and X. We ascribed the normal levels of factor VIII and fibrinogen to the fact that she was immediately post-partum, a time when the levels of these factors are apt to be very elevated. The response to heparin therapy was, at best, minimal although she seemed to do well clinically. Of note is the protracted thrombocytopenia even with heparin therapy. The explanation for this is entirely obscure.

The third case was an elderly man who exhibited easy bruising as a presenting sign. Thrombocytopenia was not present, nor was there a depression of any clotting factor other than fibrinogen. His recovery from the bruising coincided with the administration of estrogen. It is by no means certain that the hormone affected his course at all. First, one must consider that this syndrome is apparently self-limiting in many instances. To wit, many patients do not relapse after heparin therapy is withdrawn. It may well be that this man spontaneously recovered from defibrination, or it may be that he stopped defibrinating before he entered the hospital. On the other hand, defibrination with clinically significant bleeding apparently can occur without significant depression of other clotting factors or platelets. We recently saw a patient with disseminated carcinoma who presented with severe hematuria and epistaxis in whom the only abnormality of the hemostatic mechanism was hypofibrinogenemia. She was started on heparin, and within two days her fibrinogen rose from 70 to 320 mg/100 ml of plasma.

When faced with a patient who is actively bleeding and has laboratory evidence of defibrination, it is usually necessary to make rapid a diagnosis and institute therapy. As mentioned earlier, the differential diagnosis lies between intravascular coagulation and primary fibrinolysis. As it may be extremely difficult to differentiate these, therapy is frequently instituted on the assumption that intravascular coagulation underlies the bleeding. This is done for two reasons: first, it appears to be far more frequent than primary fibrinolysis, and second, heparin is more benign than the inhibitor of fibrinolysis, e-amino caproic acid

(EACA). If heparin leads to increased bleeding, it may be rapidly neutralized by administering protamine to the patient. EACA, on the other hand, is excreted unmetabolized and there is no specific inhibitor available to neutralize its effects *in vivo*. Therefore, if the patient deteriorates following EACA, and this may take the form of thrombus formation, one is committed to a course of deleterious therapy for as long as it takes to excrete the drug. If the patient has reduced renal blood flow, which is apt to accompany severe hemorrhage, this may be many hours.

In this hospital we have administered heparin to about a dozen patients who have defibrinated. We have used 250 mg/day in patients who were not severely thrombocytopenic. One must reduce the dose in the presence of thrombocytopenia as it has been shown that platelets inhibit the effects of heparin. We usually administer the drug as a constant intravenous infusion in order to insure proper blood levels. When given in this manner, under close observation, heparin appears to be well tolerated even by bleeding patients. It is therefore our practice to give an extensive trial of heparin to these patients before trying other measures. We also give blood in order to maintain circulatory volume, but not fibrinogen, except in placental abruption. In the latter instance we have not as yet used herapin as the patients seem to do well with fibrinogen alone. If we encountered a severe case of abruption in whom delivery could not be rapidly induced, we would then administer heparin.

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THE PRESIDENT'S PAGE

Compac, once a topic for debate, has now matured. By its very nature and because its accomplishmens would be largely neutralized by publication it is not debatable. The Connecticut Medical Political Committee is a reality, a very important and effective modality. Some people feel that the cause of the privately practicing physician is lost, for health is now a "public utility". They contend that the legislative arena is overrun by political opportunists who are playing havoc with the taxpayers funds and swamping our profession with myriad programs. Much of this may be true.

On the other hand, there is a positive course of action we can take if we are to preserve the American system of medical care — the best system by far in the world today. The Connecticut Medical Political Action Committee had its first major contest last year — and won its spurs. A large majority of the candidates whose campaigns it supported were successful — and they represented both parties.

Maybe it's hard to realize, because of our very dedication to the voluntary way of life, that we must unite whole-heartedly in our effort to put legislators in Hartford and in Washington who will help develop sound innovations in health care, with the advice and cooperation of those best versed in the field: the physicians.

Political philosophy and integrity aid in determining which candidates are worthy of public trust. Vast sums are being "granted" for planning, comprehensive planning, even multi-state planning. Tremendous duplication of effort. Extravagant largess through creation of new high-salaried jobs or adding fat stipends to already generous salaries. Concentration of power in the upper echelons of government where health care knowledge is minimal. — And all at the taxpayers expense.

As certain politicians act as if they know what the matter is with the health care in dear old U.S.A., so in *Man of LaMancha* Dr. Carrasco thought he knew what was the matter with Don Quixote. "Now to find the cure," quoth the padré. "May it not be worse than the disease!" We physicians must protect the public from these medico-political quacks. COMPAC has done as well with its resources as any state PAC. Not only are some funds shared with the American Medical Political Action Committee, but support is also received from AMPAC in the most politically expedient places and races. Although small, Connecticut is a key area and needs both internal and external support. AMPAC participated in 146 national races for seats in both houses of congress last year, and over 80 per cent of their candidates were victorious. No longer can climate building or lobbying suffice. Political action must be met with political action.

Campaigns are starting now. The most effective time for spending a campaign dollar is in the next few months. Your dues to COMPAC and AMPAC can go straight toward the election of candidates. Educational expenditures like the "Series of 8" pamphlets about your community, political party structure, precinct organization, etc., come from the educational fund. The National Chamber of Commerce praised the leadership of AMPAC and feels every trade and business should develop a similar PAC. President Milford O. Rouse of the AMA at Houston said, "Medical citizenship calls for active participation in AMPAC and local and state political action groups".

Let me urge each of you to join and send in your dues promptly for yourself and your wife. You could even do a really great job for $99 by becoming a sustaining member of AMPAC and COMPAC.

"Git on board, little children,
"There's room for many a more."

E. Tremain Bradley, M.D.

FROM THE GENERAL MANAGER'S OFFICE

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SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, November 16, 1967

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Bradley, Gardner, Grendon, Polivy, Brandon, M. Caplan, Fabro, Hess, Rogol, Cramer, Egan, Abbot, Spitz, Shepard, Ayres, Petrie, Pelz, Granoff, Johnson and Roch. Also present were: Mrs. Lindquist and Dr. Richards. Absent were: Drs. Hastings, Nolan, Jacobson, Jr., Grant, Wilson and Palomba.

II. Routine Business

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members of the Society:

Joseph E. Allen, Norwich (NLCMA)—1968
Bernard L. Mills, Norwich (NLCMA)—1968
Maurice R. Moore, Norwich (NLCMA)—1968
Olga Steinecke, New London (NLCMA)—1967

Date Of Next Meeting

If the Chairman and the General Manager determine that a December meeting is necessary, a tentative date for such meeting was set for Wednesday, December 6, 1967.

III. Old, New And Special Business

Election Of Student Members

It was VOTED to elect to Student Membership ten Connecticut residents who have enrolled in American schools of medicine. A list of those elected will be published in an early issue of the Journal.

Report—Public Relations Division

It was VOTED to accept a report of the PR Division on the AMA's Community Relations Program, and to urge the component county medical associations to consider implementation of the Program at county level. In brief, the Program is designed to get more physicians and their wives involved in community activities so that they can become more effective in influencing the direction that such activities take.

Report—Exploratory Meeting On Medicaid Implementation

It was VOTED to receive as information a report filed by the President, E. Tremain Bradley, on an informal meeting held on November 9, 1967 at which he, the President-Elect, Norman H. Gardner, and the Vice-President, Stevens J. Martin, had met with representatives of the Connecticut General Life Insurance Company to discuss matters of mutual interest concerning Medicaid and the Regional Medical Program.

It was further VOTED to approve the sections (first four paragraphs with minor editing) of the report dealing with Medicaid, which suggested that a maximum number of physicians should be encouraged to participate and that an effort should be made to educate people eligible for Medicaid as to the services to which they are entitled. This could be accomplished with the aid of social workers; through the distribution of informational pamphlets; and by having physicians, on request of the Society, talk to people in poverty areas, explaining that the same medical services are available to them as to anyone else and warning them against unnecessary utilization of services on their part.

It was further VOTED to approve other sections (the last two paragraphs) of the report which suggested that the Society should participate more actively in all comprehensive health planning programs and keep abreast of same. Pursuant to this suggestion, it was VOTED to request the President and the General Manager to select a CSMS member who is serving on each of the CRMP's nine task forces, and ask these representatives of the Society to be responsible for reporting on the work of their respective task forces at a fourth Conference of County Medical Association Officers (to be arranged).

Report—Advisory Committee To State Commissioners

It was VOTED to receive as information a report filed by the Advisory Committee to the State Commissioners of Welfare, Finance and Control, which outlined some of the subjects referrable to the policy aspects of the revised Title XIX program that the Advisory Committee plans to discuss with the Commissioners. Some of these matters are: (1) The use of specific pharmacies to supply prescription items; (2) Dollar limitations on the amount that prescriptions may cost; (3) Limitation on the type of drugs which may be prescribed; (4) Limitations on the frequency with which prescriptions may be written; and (5) The determination of the appropriateness of prescriptions by anyone other than the prescribing physician. It was further VOTED to suggest to the Committee that it also discuss with the Commissioners the questions of prior authorization for obtaining consultation, and limitations on the choice of consultants by the attending physician.

Communication—CSMS Section On Urology

It was VOTED to receive as information a letter of notification to the Council that the Section on Urology has adopted a resolution as follows: (AMB 11/16/67 "D")

> "RESOLVED: That the Urology Section of the Connecticut State Medical Society recommends first dollar coverage and service benefits total coverage for (CMS) Century Contract patients, based on reasonable, usual and customary fees but *not* on a fixed fee schedule."

Pursuant to the discussion of the Section's communication, it was VOTED to restate to all members of the Society (by special letter) the CSMS policy concerning the "usual and customary charge" method as the one preferred for use by all third party payors, the reasons for same, and the long-range advantages to be realized by its support and advancement.

Endorsement—Nominee For Physician Of The Year Award

Having been apprised that Robert W. Butler, Waterbury, has been nominated by the Scovill Manufacturing Company and the Waterbury Committee on Employment of the Handicapped for the 1967 Physician's Award of the President's Committee on Employment of the Handicapped, the Council VOTED unanimously to endorse Dr. Butler's nomination for this honor. Chairman of the CSMS Committee on Occupational Health, Dr. Butler has distinguished himself in the field of rehabilitating and retraining handicapped persons so that they may pursue gainful and useful occupations.

Report—Committee On Hospitals

At the request of the Council, the Committee on Hospitals made a sampling study of the question as to what extent difficulties were being encountered in the matter of getting physicians to complete transfer forms (medical records) when patients were moved from a general hospital into an extended-care facility for further treatment. It was VOTED to accept the report of the Committee, with thanks. In brief, the report indicated that three out of four extended-care facilities were finding physicians to be cooperative in completing the required transfer forms, but that greater or lesser degrees of difficulty were being experienced by the remaining 25%. The Committee feels that physicians should be reminded that it is their important duty to complete these forms promptly, not only because it is required by Medicare regulations, but also because it is of value to the continuing care of their patients. The Committee also voices the opinion that completing the transfer forms is only one part of the over-all picture of the management of patients in extended-care facilities; that equally important is the taking of "a more generally responsible attitude toward the extended-care facilities and the patients in them."

Requests For Expenditures—Report Of Fiscal Advisory Committee

Recommendations of the Council's FAC were acted on as follows:

(a) It was VOTED to approve the recommendation of the FAC that a member of the Society (to be designated by the Chairman of the Committee on Mental Health) be authorized to attend the 14th Annual Conference of Medical Society Mental Health Representatives, March 15-16, 1968, Chicago, and to be reimbursed for usual expenses in an amount up to $203.

(b) It was VOTED to approve a recommendation of the FAC that the Committee on Mental Health be authorized to spend up to $500 ($385 for printing costs; $115 for secretarial services) for the purpose of preparing, and publishing as a supplement to the Journal, a brochure on Connecticut laws pertaining to the hospitalization of the psychiatric patient. This proposal was approved as against a second proposal of the Committee which called for the brochure to be published with semi-hard cover which, with mailing charges, would require an appropriation of at least $750.

Request—Committee On Health Careers

It was VOTED to approve a request of the Committee on Health Careers that the Committee be authorized to apply for a Federal grant (under the provisions of P.L. 89-749) in the amount of up to $20,000, such grant to be used for the purpose of producing a color film on health careers to be shown at high schools and elsewhere as an adjunct to recruiting young people into the health care field. In taking this action, however, the Council reserves the right to review the terms of the grant, if approved, and to give final approval or disapproval to accepting the grant in consideration of the conditions of participation stipulated by the government.

Appointment—Study Committee On Physicians' Fees

It was VOTED to request the Chairman to appoint an Ad Hoc Committee to study and report to the Council on the feasibility of CSMS conducting a study of physicians' fees in Connecticut.

Appointment—Study Committee On Workmen's Compensation Laws

It was VOTED to request the Chairman to appoint an Ad Hoc Committee to study the Connecticut statutes applying to Workmen's Compensation, particularly those enacted by the 1967 General Assembly which give broad powers to the Compensation Commissioners with respect to setting fees for compensation work, appointing physicians to, and dismissing them from, panels authorized to treat compensation cases, etc.

Resolution—AMA House Of Delegates

Having been apprised that a resolution will be introduced at the Houston meeting of the AMA House of Delegates, November 25-29, which calls for the AMA to "admonish the National Association of Blue Shield Plans to re-study and rescind (an) action . . . . which permits the operation of a Blue Shield Plan under an arrangement which does not include approval by a sponsoring medical society," the Council VOTED to urge the AMA Delegates from CSMS to actively support this resolution.

N.B.: *The foregoing is a summary o fthe proceedings and actions of the Council on November 16, 1967. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

SURGEON—39 years of age, Board eligible, Connecticut license. Wishes to practice with a group or associate in Connecticut, with no preference to town. Available immediately, with no military obligations.

SURGEON—37 years of age, Board eligible, Connecticut license. Wishes to associate with a group or another surgeon. Available immediately.

OBS-GYN—Board certified, 33 years of age. Presently completing military obligations. Would like to enter into a group or associate practice. Available February 1, 1968.

PATHOLOGIST—34 years of age, Board eligible, Connecticut license. Is interested in an associate pathological practice. Excellent background and training. Available now.

PATHOLOGIST—36 years of age, Board certified, Connecticut license. Interested in a group, associate or institutional practice and can be available within one month.

G.P.—Applied for Connecticut license, trained in Anesthesiology, would like to practice in a solo or associate situation. Available in March, 1968.

G.P.—34, currently completing military tour desires to locate in Connecticut. Four years' solo practice experience. Solo, association or group, emergency room, college health. Connecticut license.

PLACEMENT OPPORTUNITIES

WANTED—young internist, Board eligible or certified to associate with two other young internists in modern, fully equipped building in suburb of Hartford.

INTERNIST OR G.P.—wanted in association leading to partnership with G.P. who has "quality" family practice. Do no surgery. Am associate attending at one hospital and courtesy at second. Town of 175,000 in Connecticut. Phone 233-5554.

WANTED—qualified family doctor to take over practice 30 minutes from Hartford. No obstetrics or orthopedics. Expense-sharing and coverage arrangements with M.D. in same office building. Nearby lab and x-ray. Low price for equipment. No charge for goodwill and introductions. Leaving to specialize. Contact: Lawrence S. Carlton, M.D., 65 Maple Avenue, Collinsville, Connecticut, Telephone 693-4017.

G.P.—For limited partnership with another G.P. with eventual takeover of entire practice. Well established practice in a growing town.

OPPORTUNITY exists to take over busy general practice in Southern Connecticut city. General open staff community hospital in area. Excellent professional rapport with local physicians. Transfer of records and equipment by mutual agreement.

INDUSTRIAL PHYSICIAN for leading Southern Connecticut manufacturing plant. Modern medical facilities and equipment; staff of five nurses and one assistant M.D. Salary dependent upon experience and qualifications. Excellent fringe benefits, all medical society fees paid. Five-day, 40-hour week.

WELL ESTABLISHED ORTHOPEDIC PRACTICE for sale; excellent equipment; office near major New Haven hospitals; complete files containing case histories and many legal liability matters. Gross $45,000-$50,000 yearly.

CHIEF MEDICAL OFFICERS—Challenging opportunity for an experienced physician-executive to head up medical program for large, progressive, rapid-growth corporation. Location is in midwest, age can vary from late 30's to mid-50's. Income is open and negotiable, benefits are excellent. Company climate is stimulating.

RADIOLOGIST to associate with 3 radiologists; expanding hospital and office practice in Hartford area; remuneration: negotiable, leading to full partnership. Contact: Albert C. Hurwit, M.D., 477 Connecticut Boulevard, East Hartford, Connecticut 06108.

ESTABLISHED PEDIATRICS practice available. New owner to buy present owner's equipment and share of office building. Terms of sale negotiable. Short distance from new medical school. Excellent local hospital.

SENIOR STAFF PSYCHIATRIST, full time, residential psychiatric rehabilitation center 40 miles from New York, in desirable living area with good schools. Non-profit organization oriented to intensive, individualized electic psychotherapy. Large out-patient service also. Salary open, dependent upon experience. Benefits include major medical insurance, life insurance and pension program. For information, write Charles P. Neumann, M.D., Medical Director; The Silver Hill Foundation; Box 1177; New Canaan, Connecticut 06840.

ONE YEAR PSYCHIATRIC RESIDENCY at 3rd year level for year beginning July, 1968. AMA approved. Unique opportunity to prepare for private practice and community psychiatry. Supervised, intensive, dynamically oriented, psychotherapy emphasized. Experienced in meaningful application of psychopharmacological agents and somatotherapy. Work with adults and children in residential and out-patient setting. Stipend $14,500 per annum, with major medical insurance benefits. For information, write Charles P. Neumann, M.D., Medical Director; The Silver Hill Foundation; Box 1177, New Canaan, Connecticut 06840.

PHYSICIANS needed for full-time work in Masonic Home and Hospital, Wallingford, Connecticut. High salary, excellent benefits.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.
GEN. MANAGER'S OFFICE ....

SOCIETY-SPONSORED INSURANCE PLANS

The Connecticut State Medical Society sponsors four different group insurance plans in which all CSMS members in good standing may enroll. These plans have been screened carefully by the Committee on Medical Economics and Insurance and have been approved for sponsorship by the Council. Copies of the master contracts for the four group programs are on file at the Society's headquarters building.

The plans are:
Major Medical Disability Income—Administered by, The Arthur W. Eade Agency, Hamden, Conn.
Office Overhead Expense Group Life—Administered by Group Insurers, Inc., New Haven, Conn.

At present, these four group plans are the only ones that are Society-sponsored. They are available *exclusively* to members of the Society and require membership in good standing as a condition of enrollment.

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(a schedule not unlike timed-release medication, for example)

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Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Regroton should be used in pregnant patients or in women of childbearing potential only when, in the judgment of a physician, its use is deemed essential to the welfare of the patients; adverse reactions (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn.
Precautions: Antihypertensive therapy with Regroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue Regroton therapy two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Regroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angiitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. (B) 46-600-B
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SPECIAL ARTICLE

THE CARE OF THE PATIENT

Francis W. Peabody, M.D.

Boston

Introductory Remarks

David S. Fischer, M.D.

There are many examples of fine physicians who combine the role of both an outstanding humane clinician and good scientist. Men of this kind are to be found in our community and elsewhere, and I need not list them by name as they are well known to their colleagues. However, I would like to call attention to one who died at the height of his career just 40 years ago, and left us as a legacy an aspiring essay on "The Care of the Patient." Francis Weld Peabody was an inspiration to generations of physicians in the New England States. As an investigator, "his contributions to the clinical aspects of the vital capacity of the lungs and to the metabolism of the respiration will remain as cornerstones of these branches of knowledge. His later papers on normal bone-marrow and on the pathology of the bone marrow in pernicious anemia are permanently written into the literature of these subjects, and supplemented the investigations of his devoted friend, George Minot, in one of the most beneficent therapeutic discoveries of our time . . . It is not often that this capacity for scientific concentration is combined with keen interest in men, and in its consequence—public service. There was in Francis Peabody so much joyful youth—such abundance of vitality—that far from becoming the scientific recluse, he gave himself, with adventurous ardor, to the causes that appealed to him . . . None but those most intimately associated with him knew that he had been offered, in turn, the chairs of medicine at the University of Chicago, at Columbia, at Johns Hopkins, at Yale, and at Stanford University as well as the deanship of the Chicago University Medical School—all of them declined in order to serve Harvard as Professor of Medicine and Director of the Thorndike Memorial of the City Hospital, where he developed an institution unique in the history of clinical teaching." (Boston Medical and Surgical Journal 197:1288-1292, 1928.) Dr. Peabody personally supervised patient care and medical student instruction. His lectures and rounds were immensely popular and one of his lectures on "The Care of the Patient" became so renown, that by popular demand, it was published in the Journal of the AMA on March 19, 1927, just a few months before Dr. Peabody's untimely death at age 45 from cancer.

Although I never had the pleasure of knowing Francis Peabody, (he died before I was born), I had the privilege of studying under some of his inspired students, like William Castle, Samuel Gargill, and Hermann Blumgart, among others. I remember vividly that Dr. Blumgart carried on the Peabody tradition by giving the annual lecture on "The Care of the Patient" to the second year medical class at Harvard just before the first clinical rotation. The auditorium was packed to capacity because in addition to the second year class there were also medical students of third and fourth year classes, interns, residents, clinical faculty and practitioners in the community who had come to hear this lecture for the second, third or fourth time. It was an impressive and moving lecture, and always ended with the immortal words of Francis Weld Peabody, "The good physician knows his patient through and through, and his knowledge is bought dearly. Time, sympathy and understanding must be lavishly dispensed, but the reward is to be found in that personal bond which forms the greatest satisfaction of the practice of medicine. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient."

It is probably fortunate that systems of education are constantly under the fire of general criticism, for if education were left solely in the hands of teachers the chances are good that it would soon deteriorate. Medical education, however, is less likely to suffer from such stagnation, for whenever the lay public stops criticizing the type of modern doctor, the medical profession itself may be counted on to stir up the stagnant pool and cleanse it of its sedimentary deposit. The most common criticism made at present by older practitioners is that young graduates have been taught a great deal about the mechanism of disease, but very little about the practice of medicine—or, to put it more bluntly, they are too "scientific" and do not know how to take care of patients.

One is, of course, somewhat tempted to question how completely fitted for his life work the practitioner of the older generation was when he first entered on it, and how much the haze of time has led him to confuse what he learned in the school of medicine with what he acquired in the harder school of experience. But the indictment is a serious one and it is concurred in by numerous recent graduates, who find that in the actual practice of medicine they encounter many situations which they had not been led to anticipate and which they are not prepared to meet effectively. Where there is so much smoke, there is undoubtedly a good deal of fire, and the problem for teachers and for students is to consider what they can do to extinguish whatever is left of this smoldering distrust.

To begin with, the fact must be accepted that one cannot expect to become a skilful practitioner of medicine in the four or five years allotted to the medical curriculum. Medicine is not a trade to be learned but a profession to be entered. It is an ever widening field that requires continued study and prolonged experience in close contact with the sick. All that the medical school can hope to do is to supply the foundations on which to build. When one considers the amazing progress of science in its relation to medicine during the last thirty years, and the enormous mass of scientific material which must be made available to the modern physician, it is not surprising that the schools have tended to concern themselves more and more with this phase of the educational problem. And while they have been absorbed in the difficult task of digesting and correlating new knowledge, it has been easy to overlook the fact that the application of the principles of science to the diagnosis and treatment of disease is only one limited aspect of medical practice. The practice of medicine in its broadest sense includes the whole relationship of the physician with his patient. It is an art, based to an increasing extent on the medical sciences, but comprising much that still remains outside the realm of any science. The art of medicine and the science of medicine are not antagonistic but supplementary to each other. There is no more contradiction between the science of medicine and the art of medicine than between the science of aeronautics and the art of flying. Good practice presupposes an understanding of the sciences which contribute to the structure of modern medicine, but it is obvious that sound professional training should include a much broader equipment.

The problem that I wish to consider, therefore, is whether this larger view of the profession cannot be approached even under the conditions imposed by the present curriculum of the medical school. Can the practitioner's art be grafted on the main trunk of the fundamental sciences in such a way that there shall arise a symmetrical growth, like an expanding tree, the leaves of which may be for the "healing of the nations"?

One who speaks of the care of patients is naturally thinking about circumstances as they exist in the practice of medicine; but the teacher who is attempting to train medical students is immediately confronted by the fact that, even if he would, he cannot make the conditions under which he has to teach clinical medicine exactly similar to those of actual practice.

The primary difficulty is that instruction has to be carried out largely in the wards and dispensaries of hospitals rather than in the patient's home and the physician's office. Now the essence of the practice of medicine is that it is an intensely personal matter, and one of the chief differences between private practice and hospital practice is that the latter always tends to become impersonal. At first sight this may not appear to be a very vital point, but it is, as a matter of fact, the crux of the whole situation. The treatment of a disease may be entirely impersonal; the care of a patient must be completely personal. The significance of the intimate personal relationship between physician and patient cannot be too strongly emphasized, for in an extraordinarily large number of cases both diagnosis and treatment are directly dependent on it, and the failure of the young physician to establish this relationship accounts for much of his ineffectiveness in the care of patients.

Instruction In Treatment Of Disease

Hospitals, like other institutions founded with the highest human ideals, are apt to deteriorate into dehumanized machines, and even the physician who has the patient's welfare most at heart finds that pressure of work forces him to give most of his attention to the critically sick and to those whose diseases are a menace to the public health. In such cases he must first treat the specific disease, and there then remains little time in which to cultivate more than a superficial personal contact with the patients. Moreover, the circumstances under which the physician sees the patient are not wholly favorable to the establishment of the intimate personal relationship that exists in private practice, for one of the outstanding features of hospitalization is that it completely removes the patient from his accustomed environment. This may, of course, be entirely desirable, and one of the main reasons for sending a person into the hospital is to get him away from home surroundings, which, be he rich or poor, are often unfavorable to recovery; but at the same time it is equally important for the physician to know the exact character of those surroundings.

Everybody, sick or well, is affected in one way or another, consciously or subconsciously, by the material and spiritual forces that bear on his life, and especially to the sick such forces may act as powerful stimulants or depressants. When the general practitioner goes into the home of a patient, he may know the whole background of the family life from past experience; but even when he comes as a stranger he has every opportunity to find out what manner of man his patient is, and what kind of circumstances make his life. He gets a hint of financial anxiety or of domestic incompatibility; he may find himself confronted by a querulous, exacting, self-centered patient, or by a gentle invalid overawed by a dominating family; and as he appreciates how these circumstances are reacting on the patient he dispenses sympathy, encouragement or discipline. What is spoken of as a "clinical picture" is not just a photograph of a man sick in bed; it is an impressionistic painting of the patient surrounded by his home, his work, his relations, his friends, his joys, sorrows, hopes and fears. Now, all of this background of sickness which bears so strongly on the symptomatology is liable to be lost sight of in the hospital: I say "liable to" because it is not by any means always lost sight of, and because I believe that by making a constant and conscious effort one can almost always bring it out into its proper perspective. The difficulty is that in the hospital one gets into the habit of using the oil immersion lens instead of the low power, and focuses too intently on the center of the field.

When a patient enters a hospital, one of the first things that commonly happens to him is that he loses his personal identity. He is generally referred to, not as Henry Jones, but as "that case of mitral stenosis in the second bed on the left." There are plenty of reasons why this is so, and the point is, in itself, relatively unimportant; but the trouble is that it leads, more or less directly, to the patient being treated as a case of mitral stenosis, and not as a sick man. The disease is treated, but Henry Jones, lying awake nights while he worries about his wife and children, represents a problem that is much more complex than the pathologic physiology of mitral stenosis, and he is apt to improve very slowly unless a discerning intern happens to discover why it is that even large doses of digitalis fail to slow his heart rate. Henry happens to have heart disease, but he is not disturbed so much by dyspnea as he is by anxiety for the future, and a talk with an understanding physician who tries to make the situation clear to him, and then gets the social service worker to find a suitable occupation, does more to straighten him out than a book full of drugs and diets. Henry has an excellent example of a certain type of heart disease, and he is glad that all the staff find him interesting, for it makes him feel that they will do the best they can to cure him; but just because he is an interesting case he does not cease to be a human being with very human hopes and fears. Sickness produces an abnormally sensitive emotional state in almost every one, and in many cases the emotional state repercusses, as it were, on the organic disease. The pneumonia would probably run its course in a week, regardless of treatment, but the experienced physician knows that by quieting the cough, getting the patient to sleep, and giving a bit of encouragement, he can save his patient's strength and lift him through many distressing hours. The institutional eye tends to become focused on the lung, and it forgets that the lung is only one member of the body.

Patients Who Have "Nothing The Matter With Them"

But if teachers and students are liable to take a limited point of view even toward interesting cases of organic disease, they fall into much more serious error in their attitude toward a large group of patients who do not show objective, organic pathologic conditions, and who are generally spoken of as having "nothing the matter with them." Up to a certain point, as long as they are regarded as diagnostic problems, they command attention; but as soon as a physician has assured himself that they do not have organic disease, he passes them over lightly.

Take the case of a young woman, for instance, who entered the hospital with a history of nausea and discomfort in the upper part of the abdomen after eating. Mrs. Brown had "suffered many things of many physicians." Each of them gave her a tonic and limited her diet. She stopped eating everything that any of her physicians advised her to omit, and is now living on a little milk with a few crackers; but her symptoms persist. The history suggests a possible gastric ulcer or gallstones, and with a proper desire to study the case thoroughly, she is given a test meal, gastric analysis and duodenal intubation, and roentgen-ray examinations are made of the gastro-intestinal tract and gallbladder. All of these diagnostic methods give negative results; that is, they do not show evidence of any structural change. The case is immediately much less interesting than if it had turned out to be a gastric ulcer with atypical symptoms. The visiting physician walks by and says "Well, there's nothing the matter with her." The clinical clerk says "I did an awful lot of work on that case and it turned out to be nothing at all." The intern, who wants to clear out the ward so as to make room for some interesting cases, says "Mrs. Brown, you can send for your clothes and go home tomorrow. There really is nothing the matter with you, and fortunately you have not got any of the serious troubles we suspected. We have used all the most modern and scientific methods and we find that there is no reason why you should not eat anything you want to. I'll give you a tonic to take when you go home." Same story, same colored medicine! Mrs. Brown goes home, somewhat better for her rest in new surroundings, thinking that nurses are kind and physicians are pleasant, but that they do not seem to know much about the sort of medicine that will touch her trouble. She takes up her life and the symptoms return—and then she tries chiropractic, or perhaps it is Christian science.

It is rather fashionable to say that the modern physician has become "too scientific." Now, was it too scientific, with all the stomach tubes and blood counts and roentgen-ray examinations? Not at all. Mrs. Brown's symptoms might have been due to a gastric ulcer or to gallstones, and after such a long course it was only proper to use every method that might help to clear the diagnosis. Was it, perhaps, not scientific enough? The popular conception of a scientist as a man who works in a laboratory and who uses instruments of precision is as inaccurate as it is superficial, for a scientist is known, not by his technical processes, but by his intellectual processes; and the essence of the scientific method of thought is that it proceeds in an orderly manner toward the establishment of a truth. Now the chief criticism to be made of the way Mrs. Brown's case was handled is that the staff was contented with a half truth. The investigation of the patient was decidedly unscientific in that it stopped short of even an attempt to determine the real cause of the symptoms. As soon as organic disease could be excluded the whole problem was given up, but the symptoms persisted. Speaking candidly, the case was a medical failure in spite of the fact that the patient went home with the assurance that there was "nothing the matter" with her.

A good many "Mrs. Browns," male and female, come to hospitals, and a great many more go to private physicians. They are all characterized by the presence of symptoms that cannot be accounted for by organic disease, and they are all liable to be told that they have "nothing the matter" with them. Now my own experience as a hospital physician has been rather long and varied, and I have always found that, from my point of view, hospitals are particularly interesting and cheerful places; but I am fairly certain that, except for a few low grade morons and some poor wretches who want to get in out of the cold, there are not many people who become hospital patients unless there is something the matter with them. And, by the same token, I doubt whether there are many people, except for those stupid creatures who would rather go to the physician than go to the theater, who spend their money on visiting private physicians unless there is something the matter with them. In hospital and in private practice, however, one finds this same type of patient, and many physicians whom I have questioned agree in saying that, excluding cases of acute infection, approximately half of their patients complained of symptoms for which an adequate organic cause could not be discovered. Numerically, then, these patients constitute a large group, and their fees go a long way toward spreading butter on the physician's bread. Medically speaking, they are not serious cases as regards prospective death, but they are often extremely serious as regards prospective life. Their symptoms will rarely prove fatal, but their lives will be long and miserable, and they may end by nearly exhausting their families and friends. Death is not the worst thing in the world, and to help a man to a happy and useful career may be more of a service than the saving of life.

Physiologic Disturbances From Emotional Reactions

What is the matter with all these patients? Technically, most of them come under the broad heading of the "psychoneuroses"; but for practical purposes many of them may be regarded as patients whose subjective symptoms are due to disturbances of the physiologic activity of one or more organs or systems. These symptoms may depend on an increase or a decrease of a normal function, on an abnormality of function, or merely on the subjects becoming conscious of a wholly normal function that normally goes on unnoticed; and this last conception indicates that there is a close relation between the appearance of the symptoms and the threshold of the patient's nervous reactions. The ultimate causes of these disturbances are to be found, not in any gross structural changes in the organs involved, but rather in nervous influences emanating from the emotional or intellectual life, which, directly or indirectly, affect in one way or another organs that are under either voluntary or involuntary control.

Every one has had experiences that have brought home the way in which emotional reactions affect organic functions. Some have been nauseated while anxiously waiting for an important examination to begin, and a few may even have vomited; others have been seized by an attack of diarrhea under the same circumstances. Some have had polyuria before making a speech, and others have felt thumping extrasystoles or a pounding tachycardia before a football game. Some have noticed rapid shallow breathing when listening to a piece of bad news, and others know the type of occipital headache, with pain down the muscles of the back of the neck, that comes from nervous anxiety and fatigue.

These are all simple examples of the way that emotional reactions may upset the normal functioning of an organ. Vomiting and diarrhea are due to abnormalities of the motor function of the gastrointestinal tract—one to the production of an active reversed peristalsis of the stomach and a relaxation of the cardiac sphincter, the other to hyperperistalsis of the large intestine. The polyuria is caused by vasomotor changes in renal circulation, similar in character to the vasomotor changes that take place in the peripheral vessels in blushing and blanching of the skin, and in addition there are quite possibly associated changes in the rate of blood flow and in blood pressure. Tachycardia and extrasystoles indicate that not only the rate but also the rhythm of the heart is under a nervous control that can be demonstrated in the intact human being as well as in the experimental animal. The ventilatory function of the respiration is extraordinarily subject to nervous influences; so much so, in fact, that the study of the respiration in man is associated with peculiar difficulties. Rate, depth and rhythm or breathing are easily upset by even minor stimuli, and in extreme cases the disturbance in total ventilation is sometimes so great that gaseous exchange becomes affected. Thus, I remember an emotional young woman who developed a respiratory neurosis with deep and rapid breathing, and expired so much carbon dioxide that the symptoms of tetany ensued. The explanation of the occipital headaches and of so many pains in the muscles of the back is not entirely clear, but they appear to be associated with changes in muscular tone or with prolonged states of contraction. There is certainly a very intimate correlation between mental tenseness and muscular tenseness, and whatever methods are used to produce mental relaxation will usually cause muscular relaxation, together with relief of this type of pain. A similar condition is found in the so-called writers' cramp, in which the painful muscles of the hand result, not from manual work, but from mental work.

One might go on much further, but these few illustrations will suffice to recall the infinite number of ways in which physiologic functions may be upset by emotional stimuli, and the manner in which the resulting disturbances of function manifest themselves as symptoms. These symptoms, although obviously not due to anatomic changes, may, nevertheless, be very disturbing and distressing, and there is nothing imaginary about them. Emotional vomiting is just as real as the vomiting due to pyloric obstruction, and so-called "nervous headaches" may be as painful as if they were due to a brain tumor. Moreover, it must be remembered that symptoms based on functional disturbances may be present in a patient who has, at the same time, organic disease, and in such cases the determination of the causes of the different symptoms may be an extremely difficult matter. Every one accepts the relationship between the common functional symptoms and nervous reactions, for convincing evidence is to be found in the fact that under ordinary circumstances the symptoms disappear just as soon as the emotional cause has passed. But what happens if the cause does not pass away? What if, instead of having to face a single three-hour examination, one has to face a life of being constantly on the rack? The emotional stimulus persists, and continues to produce the disturbances of function. As with all nervous reactions, the longer the process goes on, or the more frequently it goes on, the easier it is for it to go on. The unusual nervous track becomes an established path. After a time, the symptom and the subjective discomfort that it produces come to occupy the center of the picture, and the causative factors recede into a hazy background. The patient no longer thinks "I cannot stand this life," but he says out loud "I cannot stand this nausea and vomiting. I must go to see a stomach specialist."

Quite possibly the comment on this will be that the symptoms of such "neurotic" patients are well known, and they ought to go to a neurologist or a psychiatrist and not to an internist or a general practitioner. In an era of internal medicine, however, which takes pride in the fact that it concerns itself with the functional capacity of organs rather than with mere structural changes and which has developed so many "functional tests" of kidneys, heart, and liver, is it not rather narrow minded to limit one's interest to those disturbances of function which are based on anatomic abnormalities? There are other reasons, too, why most of these "functional" cases belong to the field of general medicine. In the first place, the differential diagnosis between organic disease and functional disturbance is often extremely difficult, and it needs the broad training in the use of general clinical and laboratory methods which forms the equipment of the internist. Diagnosis is the first step in treatment. In the second place, the patients themselves frequently prefer to go to a medical practitioner rather than to a pyschiatrist, and in the long run it is probably better for them to get straightened out without having what they often consider the stigma of having been "nervous" cases. A limited number, it is true, are so refractory or so complex that the aid of the psychiatrist must be sought, but the majority can be helped by the internist without highly specialized psychologic technic, if he will appreciate the significance of functional disturbances and interest himself in their treatment. The physician who does take these cases seriously—one might say scientifically—has the great satisfaction of seeing some of his patients get well, not as the result of drugs or as the result of the disease having run its course, but as the result of his own individual efforts.

Here, then, is a great group of patients in which it is not the disease but the man or the woman who needs to be treated. In general hospital practice physicians are so busy with the critically sick, and in clinical teaching are so concerned with training students in physical diagnosis and attempting to show them all the types of organic disease, that they do not pay as much attention as they should to the functional disorders. Many a student enters practice having hardly heard of them except in his course in psychiatry, and without the faintest conception of how large a part they will play in his future practice. At best, his method of treatment is apt to be a cheerful reassurance combined with a placebo. The successful diagnosis and treatment of these patients, however, depends almost wholly on the establishment of that intimate personal contact between physician and patient which forms the basis of private practice. Without this, it is quite impossible for the physician to get an idea of the problems and troubles that lie behind so many functional disorders. If students are to obtain any insight into this field of medicine, they must also be given opportunities to build up the same type of personal relationship with their patients.

Student's Opportunity In The Hospital

Is there, then, anything inherent in the conditions of clinical teaching in a general hospital that makes this impossible? Can you form a personal relationship in an impersonal institution? Can you accept the fact that your patient is entirely removed from his natural environment and then reconstruct the background of environment from the history, from the family, from a visit to the home or workshop, and from the information obtained by the social service worker? And while you are building up this environmental background, can you enter into the same personal relationship that you ought to have in private practice? If you can do all this, and I know from experience that you can, then the study of medicine in the hospital actually becomes the practice of medicine, and the treatment of disease immediately takes its proper place in the larger problem of the care of the patient.

When a patient goes to a physician he usually has confidence that the physician is the best, or at least the best available person to help him in what is, for the time being, his most important trouble. He relies on him as on a sympathetic adviser and a wise professional counselor. When a patient goes to a hospital he has confidence in the reputation of the institution, but it is hardly necessary to add that he also hopes to come into contact with some individual who personifies the institution and will also take a human interest in him. It is obvious that the first physician to see the patient is in the strategic position—and in hospitals all students can have the satisfaction of being regarded as physicians.

Here, for instance, is a poor fellow who has just been jolted to the hospital in an ambulance. A string of questions about himself and his family have been fired at him, his valuables and even his clothes have been taken away from him, and he is wheeled into the ward on a truck, miserable, scared, defenseless and, in his nakedness, unable to run away. He is lifted into a bed, becomes conscious of the fact that he is the center of interest in the ward, wishes that he had stayed at home among friends, and, just as he is beginning to take stock of his surroundings, finds that a thermometer is being stuck under his tongue. It is all strange and new, and he wonders what is going to happen next. The next thing that does happen is that a man in a long white coat sits down by his bedside, and starts to talk to him. Now it happens that according to our system of clinical instruction that man is usually a medical student. Do you see what an opportunity you have? The foundation of your whole relation with that patient is laid in those first few minutes of contact, just as happens in private practice. Here is a worried, lonely, suffering man, and if you begin by approaching him with sympathy, tact, and consideration, you get his confidence and he becomes your patient. Interns and visiting physicians may come and go, and the hierarchy gives them a precedence; but if you make the most of your opportunities he will regard you as his personal physician, and all the rest as mere consultants. Of course, you must not drop him after you have taken the history and made your physical examination. Once your relationship with him has been established, you must foster it by every means. Watch his condition closely and he will see that you are alert professionally. Make time to have little talks with him—and these talks need not always be about his symptoms. Remember that you want to know him as a man, and this means you must know about his family and friends, his work and his play. What kind of a person is he—cheerful, depressed, introspective, careless, conscientious, mentally keen or dull? Look out for all the little incidental things that you can do for his comfort. These, too, are a part of "the care of the patient." Some of them will fall technically in the field of "nursing" but you will always be profoundly grateful for any nursing technic that you have acquired. It is worth your while to get the nurse to teach you the right way to feed a patient, change the bed, or give a bed pan. Do you know the practical tricks that make a dyspneic patient comfortable? Assume some responsibility for these apparently minor points and you will find that it is when you are doing some such friendly service, rather than when you are a formal questioner, that the patient suddenly starts to unburden himself, and a flood of light is thrown on the situation.

Meantime, of course, you will have been active along strictly medical lines, and by the time your clinical and laboratory examinations are completed you will be surprised at how intimately you know your patient, not only as an interesting case but also as a sick human being. And everything you have picked up about him will be of value in the subsequent handling of the situation. Suppose, for instance, you find conclusive evidence that his symptoms are due to organic disease; say, to a gastric ulcer. As soon as you face the problem of laying out his regimen you find that it is one thing to write an examination paper on the treatment of gastric ulcer and quite another thing to treat John Smith who happens to have a gastric ulcer. You want to begin by giving him rest in bed and a special diet for eight weeks. Rest means both nervous and physical rest. Can he get it best at home or in the hospital? What are the conditions at home? If you keep him in the hospital, it is probably good for him to see certain people, and bad for him to see others. He has business problems that must be considered. What kind of a compromise can you make on them? How about the financial implications of eight weeks in bed followed by a period of convalescence? Is it, on the whole, wiser to try a strict regimen for a shorter period, and, if he does not improve, take up the question of operation sooner than is in general advisable? These, and many similar problems arise in the course of the treatment of almost every patient, and they have to be looked at, not from the abstract point of view of the treatment of the disease, but from the concrete point of view of the care of the individual.

Suppose, on the other hand, that all your clinical and laboratory examinations turn out entirely negative as far as revealing any evidence of organic disease is concerned. Then you are in the difficult position of not having discovered the explanation of the patient's symptoms. You have merely assured yourself that certain conditions are not present. Of course, the first thing you have to consider is whether these symptoms are the result of organic disease in such an early stage that you cannot definitely recognize it. This problem is often extremely perplexing, requiring great clinical experience for its solution, and often you will be forced to fall back on time in which to watch developments. If, however, you finally exclude recognizable organic disease, and the probability of early or very slight organic disease, it becomes necessary to consider whether the symptomatology may be due to a functional disorder which is caused by nervous or emotional influences. You know a good deal about the personal life of your patient by this time, but perhaps there is nothing that stands out as an obvious etiologic factor, and it becomes necessary to sit down for a long intimate talk with him to discover what has remained hidden.

Sometimes it is well to explain to the patient, by obvious examples, how it is that emotional states may bring about symptoms similar to his own, so that he will understand what you are driving at and will cooperate with you. Often the best way is to go back to the very beginning and try to find out the circumstances of the patient's life at the time the symptoms first began. The association between symptoms and cause may have been simpler and more direct at the onset, at least in the patient's mind, for as time goes on, and the symptoms become more pronounced and distressing, there is a natural tendency for the symptoms to occupy so much of the foreground of the picture that the background is completely obliterated. Sorrow, disappointment, anxiety, self-distrust, thwarted ideals or ambitions in social, business or personal life, and particularly what are called maladaptations to these conditions —these are among the commonest and simplest factors that initiate and perpetuate the functional disturbances. Perhaps you will find that the digestive disturbances began at the time the patient was in serious financial difficulties, and they have recurred whenever he is worried about money matters. Or you may find that ten years ago a physician told the patient he had heart disease, cautioning him "not to worry about it." For ten years the patient has never mentioned the subject, but he has avoided every exertion, and has lived with the idea that sudden death was in store for him. You will find that physicians, by wrong diagnoses and ill considered statements, are responsible for many a wrecked life, and you will discover that it is much easier to make a wrong diagnosis than it is to unmake it. Or, again, you may find that the pain in this woman's back made its appearance when she first felt her domestic unhappiness, and that this man's headaches have been associated, not with long hours of work, but with a constant depression due to unfulfilled ambitions. The causes are manifold and the manifestations protean. Sometimes the mechanism of cause and effect is obvious; sometimes it becomes apparent only after a very tangled skein has been unraveled.

If the establishment of an intimate personal relationship is necessary in the diagnosis of functional disturbances, it becomes doubly necessary in their treatment. Unless there is complete confidence in the sympatheic understanding of the physician as well as in his professional skill, very little can be accomplished; but granted that you have been able to get close enough to the patient to discover the cause of the trouble, you will find that a general hospital is not at all an impossible place for the treatment of functional disturbances. The hospital has, indeed, the advantage that the entire reputation of the institution, and all that it represents in the way of facilities for diagnosis and treatment, go to enhance the confidence which the patient has in the individual physician who represents it. This gives the very young physician a hold on his patients that he could scarcely hope to have without its support. Another advantage is that hospital patients are removed from their usual environment, for the treatment of functional disturbances is often easier when patients are away from friends, relatives, home, work and, indeed, everything that is associated with their daily life. It is true that in a public ward one cannot obtain complete isolation in the sense that this is a part of the Weir Mitchell treatment, but the main object is accomplished if one has obtained the psychologic effect of isolation which comes with an entirely new and unaccustomed atmosphere. The conditions, therefore, under which you, as students, come into contact with patients with functional disturbances are not wholly unfavorable, and with very little effort they can be made to simulate closely the conditions in private practice.

Importance Of Personal Relationship

It is not my purpose, however, to go into a discussion of the methods of treating functional disturbances, and I have dwelt on the subject only because these cases illustrate so clearly the vital importance of the personal relationship between physician and patient in the practice of medicine. In all your patients whose symptoms are of functional origin, the whole problem of diagnosis and treatment depends on your insight into the patient's character and personal life, and in every case of organic disease there are complex interactions between the pathologic processes and the intellectual processes which you must appreciate and consider if you would be a wise clinician. There are moments, of course, in cases of serious illness when you will think solely of the disease and its treatment; but when the corner is turned and the immediate crisis is passed, you must give your attention to the patient. Disease in man is never exactly the same as disease in an experimental animal, for in man the disease at once affects and is affected by what we call the emotional life. Thus, the physician who attempts to take care of a patient while he neglects this factor is as unscientific as the investigator who neglects to control all the conditions that may affect his experiment. The good physician knows his patients through and through, and his knowledge is bought dearly. Time, sympathy and understanding must be lavishly dispensed, but the reward is to be found in that personal bond which forms the greatest satisfaction of the practice of medicine. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.

TAX EXEMPTIONS FOR BLIND PERSONS

State Senator George L. Gunther (21st District) suggests that practitioners throughout Connecticut might be interested in the following statutory benefit available to blind persons coming under their care:

SECTION 12-81 PROPERTY TAX EXEMPTIONS

(17) *Blind Persons.* Subject to the provisions of sections 12-89, 12-90 and 12-92, property to the amount of three thousand dollars belonging to, or held in trust for, any blind person, resident of this state; or lacking said amount of property in his own name, so much of the property belonging to, or held in trust for, his spouse, who is domiciled with him, as is necessary to equal said amount; . . . .

SECTION 12-92

Proofs To Be Filed By Blind. No individual shall receive any exemption to which he is entitled by subdivision (17) of Section 12-81 until he or his authorized agent or attorney has given proof satisfactory to the board of assessors that he is blind. . . . For the purposes of subdivision (17) of Section 12-81 and this Section, blindness shall be defined to mean total and permanent loss of sight in both eyes or reduction in vision so that central visual acuity does not exceed 20/200 in the better eye with corrective lenses, or, if visual acuity is greater than 20/200, it is accompanied by a limitation in the fields of vision such that the widest diameter of the visual field subtends an angle no greater than twenty degrees.

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SUMMARY OF PROCEEDINGS
HOUSE OF DELEGATES — SEMI-ANNUAL MEETING

Groton Connecticut — December 13, 1967

REPORTS AND ADDRESSES

The House received reports and/or addresses from the President, the Treasurer, the Chairman of the Council, the AMA Delegates, the General Manager and the Chairman of the Board of Directors of COMPAC. The address of the President and several other reports are published at the end of this summary.

MAJOR ACTIONS TAKEN

1968 Budget

It was VOTED to adopt the budget for 1968, prepared and approved by the Council, and to continue membership dues at the 1967 level of $50.00.

Amendments to the Bylaws re "Judicial Committee"

It was VOTED to defer final action on amendments to establish a "Judicial Committee", on the table since the April meeting, and to approve the report of Reference Committee A that the study of the amendments begun by the Reference Committee be continued by an Ad Hoc Committee to be appointed by the President, and that the Ad Hoc Committee submit a report, with recommendations, on this subject to the 1968 Annual Meeting of the House.

Resolution on Usual and Customary Charges

Introduced by the Section on Pediatrics, it was VOTED to adopt a resoluion as follows:

* "RESOLVED: That (with respect to the Title XIX Program of Medical Assistance) the Connecticut State Medical Society continue to use all of its resources to assure the success of the system of usual and customary charges."

Resolution re "Challenge" to the AMA

Having been informed that a splinter organization of physicians and others (with national and state chapters) has issued a public "challenge" to the American Medical Association to change its positions, or adopt new positions, on a number of medical socio-economic matters, the House of Delegates adopted the following resolution concerning the mechanisms which are available to all members of organized medicine to influence all positions of the AMA and its state and county subdivisions:

"Resolved: That the House of Delegates of the Connecticut State Medical Society reaffirm its conviction that the official positions of the Society and/or the American Medical Association reflect the views of a majority of the members thereof; and be it further

RESOLVED: That the House of Delegates of the Connecticut State Medical Society reaffirm its confidence in the existing mechanisms provided by organized medicine that operate to afford all participating members the opportunity to make their views known, either by direct vote or through duly elected representatives; and be it further

RESOLVED: That the House of Delegates recall to every member of the Connecticut State Medical Society his or her guaranteed right to submit recommendations which would establish, amend or rescind official positions of the Society and/or the American Medical Association, and to engage in all legitimate political and legislative activities within the organizations which are directed toward gaining majority approval of such recommended positions."

Authorization to Form New Section

It was VOTED to authorize the formation of a Section on Thoracic and Cardiovascular Surgery.

Educational Grant to COMPAC

Having heard the favorable recommendation of the Council, and representative reports that seven of the eight component county medical associations favored the action, it was VOTED to approve a 1968 education grant to the Connecticut Medical Political Action Committee (listed as an identifiable item in the budget for 1968). As in prior years, it is stipulated that these grant funds are to be used by COMPAC *only* for educational activities designed to stimulate greater participation in political affairs by physicians and their wives and families.

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*The usual and customary charge method of payment for physicians' services will be used during a year's trial period (March 1, 1968 — March 1, 1969) by the Welfare Department under the Title XIX Program (Medicaid).

COMPAC Dues Billings

Two related actions were taken by the House which concerned the mailing out of COMPAC membership dues billings in conjunction with dues statements of the Society and the County Medical Association as follows:

(a) It was VOTED to amend a resolution previously adopted by the House of Delegates (12/9/65) so that COMPAC dues billings may be included *with* the membership dues statements of the Society and the County Medical Associations, instead of *on* such statements (as stipulated originally).

(b) It was VOTED (pursuant to the previous action) to request the Board of Directors of COMPAC to furnish the Society and the Hartford County Medical Association with COMPAC billing forms for inclusion with dues statements of CSMS and HCMA.

Confirmation of Interim Appointments

It was VOTED to confirm a series of appointments made, and resignations accepted, by the Council since the April meeting of the House of Delegates. Among these was the appointment of Frank K. Abbot, Waterbury, as Vice-Speaker of the House, to complete the unexpired 1967-68 term of Henry Caplan, Yalesville, resigned.

Further Amendments to the Bylaws

Placed on the table, without discussions, were a series of Council-recommended changes in the bylaws concerning: The Committee on Publications; The Committee on AMA-ERF; The Advisory Committee to the State Commissioners of Welfare, Finance and Control; the Committee on Postgraduate Education; and the Delegates to the Council of N.E. State Medical Societies. These will be published one or more times in the Journal, and be acted upon at the 1968 Annual Meeting of the House of Delegates.

REMARKS OF THE PRESIDENT

E. Tremain Bradley, Norwalk

Mr. Speaker, members of the House, welcome guests.

Today again the machinery of reference committees has been but to active use. Those who attended found satisfaction in this opportunity to express themselves on matters of importance to the Society. But beyond this, they had the privilege of hearing the free expression of thought and reason — and even emotion — by others on the same subjects. Now when the reports of the reference committees emerge from the executive sessions and are presented on the floor of this House, the delegates will be in much better position to vote intelligently than prior to this communicating. We are looking forward to a further expansion of the use of reference committees at the annual meeting next Spring. This will mean spreading the activities of the House over a two day period. Thus, the work will be done more deliberately and the results should be better. Also, there will be opportunity for those attending the House of Delegates to attend some of the scientific sessions more easily, and likewise the Society members attending scientific sessions will be on hand to attend and even participate in the reference committee hearings. We need the ideas and intelligence of our entire membership, and I am sure we can count on full cooperation with this necessary innovation. I say we need all the intelligence of all our membership, in the pursuit of our goal: seeing to it that our patients — that is, the public as a whole — are provided the best health care possible at a reasonable price.

Until recently, we have concentrated on care of the individual sick person, the control of epidemics, and certain public health measures. Now the number of studies and treatments available are astronomical — and of course the cost has risen accordingly. We must, therefore, search the horizon and beyond through a wide-angle lens.

There is a real danger not only to private enterprise but to freedom itself today. Many people are demanding that the government do for them what only they can do for themselves. They demand their "rights". What do we mean by "rights"? When lecturing to the medical students at Yale by invitation recently, someone asked what a person's rights were. I don't believe anyone really has any rights other than those which are earned, or those which leave the individual in debt. One earns the right to breath by making the effort. When one studies to become a doctor and learns from the experience and efforts of those who have gone before him, he immediately becomes indebted to the future and should pay this debt by helping to educate doctors of the future. With the advent of government subsidy of medical care, the patients who were being treated gratis are no longer present and available for use in teaching programs. This has caused consternation in many quarters. I find no need for such consternation. Every patient who has the "right" to medical care is getting this care because some previous patients have contributed to a teaching program. Therefore, every patient today who receives medical care owes it to future patients to cooperate in teaching programs wherever indicated. Naturally, the safety and well-being of the patient must always be protected. Actually, it has often been in the past that the free patients on a teaching service received more attention and at times even more careful care than the average patient. Whenever a patient is admitted to a hospital, a statement is signed allowing the hospital and physicians to take care of the patient. It would be both simple enough and logical enough to add to this statement that the patient is willing to cooperate reasonably in any teaching program. One should be just as much a pre-requisite to admission to a hospital as the other. This would in no wise diminish the privilege or responsibility of the patient's personal attending physician.

There may not have been enough planning for the improvement of health care and the financial efficiency of its provisions. Now we have a plethora. Planning groups — federal, state, voluntary and private — have sprung up and are stumbling over each other — stumbling at tremendous expense to the taxpayer. The amount of participation sought from or permitted to physicians in this planning varies but is mostly quite limited. Whoever controls the purse strings usually likes to keep control of them. Considerable legislation has already been enacted, much of it with very little advice taken from those who know most about the subject. We must not be obstructive, but should be eager for an orderly, progressive, meaningful change. The cost of hospital care can be diminished by emphasizing ambulatory and home care. Incidentally, did you see on the front page of the New York Times recently an article reporting that the doctors had been criticized by labor leader George Meany because their fees had risen 8 per cent. It was interesting that one of his own unions, at that very time, was on strike demanding a 30 per cent wage rise. In the AMA News for November '65, an entire page was devoted to the future roles of group practice. In some areas, hospital staffs are incorporating. Yet no one system is going to be satisfactory for all parts of the country. If there are to be joint ventures between government or lay organizations and physicians, there must be mutual respect and cooperation. Federal laws should outline purpose and principle, primarily. Too much emphasis cannot be placed on the importance of local control of programs, so that the resources peculiar to the locality can be harnessed and driven by a coachman who knows the neighborhood roads; so that neither time nor energy is lost or substance wasted.

The Medical Society should act in an advisory and promotional capacity, but would do well to avoid the operational. The acceptance of finances often enforces subservience to rules and regulations of the donor. We should certainly cooperate *with* government, but not work *for* it. In this land of free enterprise, the availability of government funds must not allow to deteriorate the provision of medical care. No contractual arrangement should by-pass participation of the local medical societies.

In any joint venture, there should be mutual respect. This holds for relationships between the Society and the government or hospital boards or third party agencies. Relations with the Commissioner of Welfare have taken leaps forward. Much mutual respect was engendered when our Society met with the legislators to discuss the significance of Title XIX in Hartford last Spring. Many more hospitals are including physicians on their Board of Trustees with a right to vote. Isn't it a shame that the doors were not open for the Medical Society to point out the advantages of the usual and customary charges method to a Blue Shield that could have been much more useful to the people of Connecticut. Some mutual respect and willingness to listen to the other side might have ended up in progressive leadership. You have all recently received a letter on yellow paper which outlines quite specifically the principles for which the Society stands. I hope you will read it carefully and if there are any doubts or questions in your minds, I trust you will contact one of the three signators.

You might be interested to know that at the recent meeting of the House of Delegates in Houston, a resolution was introduced from Iowa, and was passed, requesting the National Blue Shield to reconsider its actions last June eliminating sponsorship by a medical society as a requirement for membership. Their representative who spoke in the reference committee seemed more than willing to return the matter for reconsideration, along with a recommendation for consultation with both sides in any dispute.

Cooperation between specialty groups and the Society has improved, with some forming sections in the Society, almost but not quite identical with the specialty organization. In this manner, we can understand each other better and present a united effort toward improving health care and keeping costs down.

Attempts to establish minimum standards of care present a problem similar to having universal directives of care established federally. How often is a patient or a situation "standard"? Actually, the competence, service and ethics of a physician are constantly under review by his peers: in clinical pathological conferences, by utilization review committees, beore Boards of Censors, and so on. Laws don't make a good doctor nor deliver good medical service. This only comes from an inner desire to be honest and from insisting on the integrity of those around us. We want our work to be good and welcome constructive criticism which will help both us and our patients.

Early next year, we anticipate holding the fourth Conference of County Medical Association Officers, probably on the subject of the Connecticut Regional Medical Plan. These have been highly successful, instructive and enjoyable sessions. You will be interested to know that at Houston, an interstate gathering of county medical association officers was approved by the House.

Our Public Relations Department has sponsored diabetes detection programs in some underprivileged areas with apparent fine reception. We are cooperating in educational programs concerning Title XIX. It is, of course, helpful for physicians to be aware of the various benefits which their patients may be entitled to, and to help them collect from whatever agency is supplying these benefits. However, it would be impossible for each of us to be aware of every benefit available to any patient who comes to us. The people who create the laws or regulations are, in the last analysis, responsible for being sure that the people they are trying to benefit are aware of the benefits available to them. A patient with renal transplant was denied benefits of some $13,000 by the Department of Rehabilitation because there had not been prior authorization. We should try to help our patients avoid this hardship but we should work to eradicate the unfair prior authorization.

Talk about planning: We must prepare now for the sensible changes, improvements and deletions which we feel should be made in the statutes. This has to be done through legislators, and that means we must have legislators who are well-in-formed and who are sympathetic to the principles of the best possible medical care at a reasonable cost under the free enterprise system. The Connecticut Medical Political Action Committee — COMPAC to you — made an outstanding record in the past election and the result showed in the General Assembly this Spring. COMPAC has done as well as any PAC with the resources it has — in both national and state elections. COMPAC is our political arm. If we want the proper method of practice and through this the proper care of our patients in the future, we must have the right laws and so we must support COMPAC — not just with educational grants, though that is important, too, but through active membership by each one of us here and by active encouragement of our constituents at home to enter into this very vital project. I know there are personal prejudices but I hope each of us is big enough to overlook these for the common good — both of the medical profession and of the public at large.

In addition to supplementing the thoughts which have come to you in my President's Page each month, and, unfortunately the November and December issues of *Connecticut Medicine,* with their special messages, have been delayed by strike, these remarks are presented on behalf of the officers of your Society. It gives me great pleasure to present them to you at this time. Your President-Elect has served you for some years as Delegate to the AMA, Norman H. Gardner. Dr. Gardner, would you please stand and be recognized. Our Vice-President also does double duty He wields the whip as Chairman of the Council and does a difficult job pleasantly and efficiently, Dr. Stevens J. Martin. Dr. Martin, will you please stand and be recognized. Our Treasurer, who is Councilor from Litchfield County, is responsible for the budget which will be presented to you later, and is Chairman of the Finance Committee which invests your reserves. These are important, time-consuming and detailed tasks, Dr. David A. Grendon. Our Secretary, who was very helpful this past spring when the General Assembly was in session, Dr. Charles Polivy. Although not an officer, the Society could not run without him, the indefatigable, inscrutable, irrepressible General Manager, Dr. William R. Richards. It's impossible to tell you what a wonderful crew you have working at 160 St. Ronan St., the tireless and considerate effort which they put out constantly.

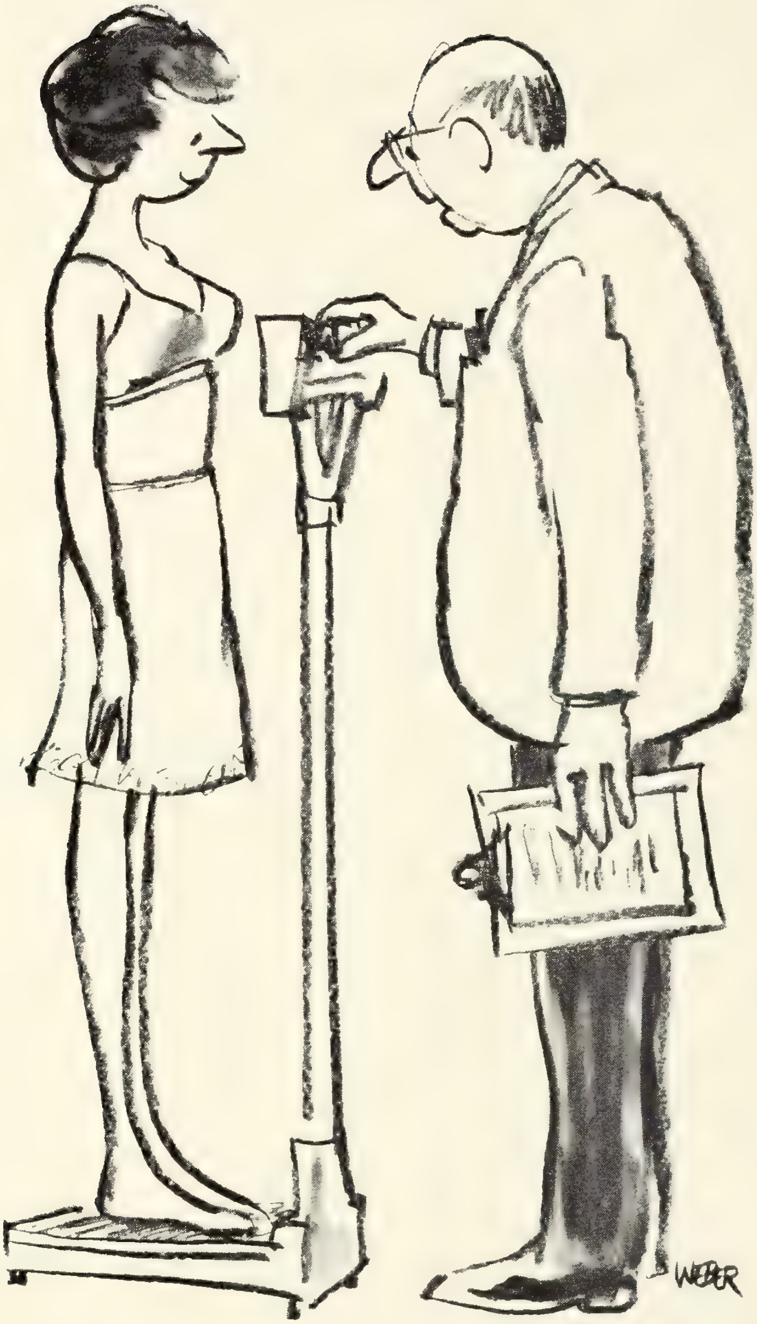
Report of the Delegates to the AMA

Norman H. Gardner

East Hampton

Houston, Texas — November 26-29, 1967

The proceedings of the House were opened by an address from Doctor Milford O. Rouse, President of the American Medical Association. He started off by saying that the future of the individual phy-



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Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.
Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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sician, of patient care and of the methods by which it will be made available to all people do not depend on our efforts alone. He felt there is also dependence on the future attitude of the nation toward free enterprise, on the degree of future national respect for individual initiative and on the extent of future over all acceptance of the concept that personal satisfaction and personal benefit are to be gained principally through personal endeavor. He stated that leaders in government see it as their duty to do for people of this country whatever they believe, or whatever they are told by citizen groups is not already being done. When private citizens abdicate their responsibilities and ask the government to do a job, government responds in the only way it can, by passing more laws. Each time this is done, it means another small or large restriction on somebody's freedom. Doctor Rouse remarked that we have a choice when facing a situation that needs correcting: we can do it ourselves; or we can ask the government to pass a law and set up an administrative mechanism to enforce it. Doctor Rouse felt that we have now reached a point where we can no longer just cling to the traditions of our distinguished past. He believes the time has come for orderly, planned, meaningful change in the material features of efficiency, cost and methods of delivery of health care. Doctor Rouse asks that we be careful not to make it necessary for anybody else to direct the furnishing of the services which the people of this country demand.

The House adopted a report of the Board of Trustees containing fifteen recommendations from the report on the Commission on Research. One of the recommendations stated that there should be allotted a greatly increased amount of governmental aid for operational expenses of medical schools. In passing this recommendation, the House asked that a definite matching formula be used to encourage medical schools to retain their independence.

In reporting on the report of the National Advisory Commission on Health Manpower which was submitted to President Johnson on November 20, the Board of Trustees pointed out that there had not been time to study and evaluate the Commission report in any depth but also noted that the Commission's approach to health care problems indicated recognition of the need for orderly procedures rather than harmful crash programs and noted that the emphasis in most of the Commission report is to center responsibility on the professional groups best able to evaluate and plan in health areas, rather than on government and non-professionals.

The House emphasized that standards of medical care are set at the local level and called attention to disturbing trends pointing to possible establishment of medical care standards on a national basis.

The House passed a resolution which commits the American Medical Association to leadership in informing the public, the profession and other elements of the health care field as to practical means of moderating health care costs, the value of voluntary health insurance, expanding the medical manpower supply and improving the health care of the American people.

The House urged State and Local Medical Societies to emphasize a variety of activities to be undertaken in the area of over all planning for governmental and private programs of health care including continued effort by the medical profession to improve federal legislation in this area and to emphasize the importance of local control.

The House reaffirmed that the procurement, processing, distribution or use of human blood and other tissue is a medical service and is not the selling of a commodity. The Board of Trustees and the State Associations were urged to support legislative action at federal and state levels to implement this concept. This latter is a resolution presented by the delegation from the Connecticut State Medical Society and was gratifying to the delegation that this was passed without change.

The use of monitoring, defibrillation and resuscitative equipment by registered nurses in cases of cardiac emergencies was approved, with provisions regarding the nurse's training and the procedures established by the hospital medical staff.

The House reaffirmed its support of direct billing for federal health care programs. It asked that the American Medical Association continue its efforts to provide for the implementation of Title XIX in a manner which recognizes the physician's right to bill directly to all patients, including Title XIX patients and allows the physician or his patient to be reimbursed his usual, customary and reasonable fee for his professional services; and that the Association actively seek changes in the law that will secure equal and simultaneous application to all jurisdictions.

A resolution was passed which proposed the acceptance of physicians on hospital Boards of Trustees as the most effective form of liaison between the medical staff and the hospital governing authorities. Also, a resolution was passed protecting hospital privileges through due process.

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1. Schleif, R.H.: J.A.PH.A., 46:179,1957 *U.S. Pat. No. 3,062,714

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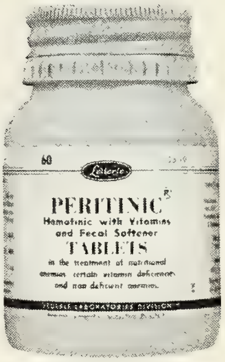

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anticostive, *adj.* (*anti* opposed to + *costive* causing constipation.) Against constipation. (Now isn't that a good idea in an iron-containing hematinic? We'll send you samples if you'll send a request on your Rx blank, addressed to Department 150.)

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A statement concerning the purposes and responsibilities of the American Medical Association was passed in its entirety reiterating that it is the responsibility of the American Medical Association, as the representative of the American Medical Profession, to continue to foster the advancement of medical science and the health of the American people through the following means:

1. By encouraging the further development of medical knowledge, skills, techniques and drugs; and by maintaining the highest standards of practice and health care.
2. By creating incentives to attract increasing numbers of capable people into medicine and other health-care professions.
3. By advancing and expanding the education of physicians and other groups in the health-care field.
4. By motivating skilled physicians who have the art of teaching to apply themselves to developing new generations of excellent practitioners.
5. By fostering programs that will encourage medical and health personnel to serve voluntarily in the areas of need for medical care.
6. By developing techniques and practices that will moderate the costs of good medical and health care.
7. By seeking out and fostering means of making all health-care facilities — physicians' officers, hospitals, laboratories, clinics and others — as efficient and economical as good medical practice and attention to human values will permit.
8. By combining the utilization of the latest knowledge for prevention and treatment with the vital healing force of the physician's personal knowledge of, and devotion to, his patients.
9. By maintaining the impetus of dedicated men and women in providing excellent health care by preserving the incentives of effectiveness of unshackled medical practice.
10. By maintaining the highest level of ethics and professional standards among all members of the medical profession.
11. By continuing to provide leadership and guidance to the medical profession of the world in meeting the health needs of changing populations.

Report of the General Manager

William R. Richards

New Haven

Mr. Speaker, Mr. President, Members of the House and Guests:

Nowadays it is almost impossible to read a newspaper without learning that some group or other is engaged in waging war on "THE ESTABLISHMENT" — the political establishment, the business establishment, the religious establishment, the moral establishment and so on. The dictionary really doesn't help us very much in understanding just what an establishment is, and, hence, each of us has to more or less make up a definition for himself.

In my view, an establishment is an individual or a group of individuals who, in a representative form of society, are authorized to say things and do things that have the support of a majority of the people falling within the jurisdictional area of the particular establishment concerned. When the support of the majority dwindles or is lost, the incumbent establishment crumbles and a new one is accredited to take its place.

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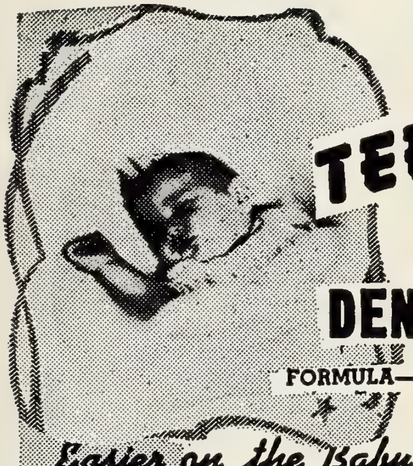

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Easier on the Baby . . .

DENTOCAIN LOTION MILD makes it easier to go through the troublesome teething period. A small amount, applied with gentle massage, brings quick, soothing relief to irritated and inflamed gum tissue, aids in getting infant back to sleep.

Easier on the Mother . . .

By providing more comfort and extra sleep for the baby, DENTOCAIN LOTION MILD grants the mother greater peace of mind and several additional hours of necessary rest.

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Professional samples and descriptive literature sent on request.

Now, organized medicine is certainly an establishment — or, rather, a series of establishments operating respectively at county, state and national levels. The members of the American Medical Association and its subdivisions who hold office are responsible for representing the American medical profession in a hundred or more different areas of scientific, educational, legislative and socioeconomic activities, and they may continue in office only so long as what they say and do meets with the over-all approval of a major segment of the membership.

In organized medicine, we also have a representative system of government. All members in good standing who wish to take an active part in their organizations' affairs are on an equal footing with all other members, having the right to speak, the right to be heard, the right to vote and the right to hold office. Hence, within the establishment of medicine it is difficult for me to understand how the views of any minority could ever prevail; how any member or any less-than-a-majority group of members could ever put anything over on the other 200,000 or so.

Yet, despite these facts of the matter — facts of which we can all be proud, we find that on many fronts our voluntary medical federations are being attacked on the grounds that — somehow — the facts "just ain't so." Often it is a politician who, in defense of his position on a particular piece of health legislation, claims publicly that he "has reason to believe that the AMA really isn't representing the views of a majority of the nation's doctors."

Less often — but far more serious in import, because they should know better — it is a small group of our colleagues that undertakes to spread this myth. "The president of the AMA doesn't speak for us!", they proclaim at a hastily called press conference, "In fact, we take issue with the AMA's positions on practically everything — and we're by no means alone in our disagreement. The Association should adopt the positions that *we* espouse!"

During the last session of the General Assembly, I had occasion to engage in a philisophical discussion of politics with a State Senator of considerable prominence and long experience as an officeholder. In essence, he said to me: "I find that the people who protest the loudest about how badly government is being run, and who profess to know better than anyone else which bills should be passed and which defeated, are more often than not people who don't belong to either political party, who don't participate in the selection of party nominees, who don't lift a finger in support of any candidate's election, who frequently don't bother to go to the polls on election day, and who — not rarely — have not even bothered to register to vote. I feel that these citizens richly deserve any kind of government they get, and, although I'm a politician through-and-through, I don't hesitate for a minute to tell them so!"

The specfic matters pertinent to this general subject that I wish to bring to the attention of the House of Delegates today are two: first, a three-quarter page ad which appeared in the December 10 issue of the *New York Times*, and, second, a news story which appeared in the *New Haven Register* on that same day. In bold print, the ad is headed: WE CHALLENGE THE AMA, and the copy goes on to severely criticize our national body on a number of counts with respect to its official positions. It is undersigned by some fifty or so physicians and a few non-physicians, members of a Medical Committee for Human Rights. In the New Haven news article, several Connecticut members of the MCHR endorse the "challenge" issued by the national body and elaborate on it with critical comments of their own.

This is neither the time nor place to delve into the specifics of the several AMA positions with which this splinter group takes issue. I feel strongly, however, that it *is* important for the House of Delegates to respond today to this "challenge" to organized medicine insofar as a major principle is concerned — the principle that we do adhere to a democratic, representative system of government in which, at any time, if supported by a majority of members, our officers, committees, policies and all else can — and will — be changed. This does not mean that any member or group of members should expect to have such changes handed to them on a platter; that just because *they* say something is so, it is necessarily so. The democratic process, in operation, characteristically calls for the application of a certain amount of elbow-grease if majority support is to be sought and gained.

Accordingly, as an ex-officio member of the House I am introducing a resolution reaffirming support of this principle. I recommend that, in keeping with our rules of procedure, the resolution be considered and acted upon under "New Business."

(The resolution adopted is reproduced under "Summary of Proceedings")

MEETINGS

BASIC SCIENCE

Every Other Tuesday 7:15 p.m.

Hematology Lecture Series

Auditorium, Lawrence and Memorial Hospitals, New London

Fee, $100 for 20 Seminars

Description: The Hematology series of courses in Basic Science as Related to Clinical Medicine is coordinated by Robert S. Schwartz, M.D., Associate Professor Medicine, Tufts University School of Medicine, and Chief, Clinical Immunology Service, New England Medical Center Hospitals. Postgraduate credit from the Connecticut Academy of General Practice granted to participants.

Program Director: Edward Gipstein, M.D., Director of Medical Education, Lawrence and Memorial Hospitals. (442-0711 Ext. 361)

Limited to 75 registrants

MEDICINE

March 27 9:30 a.m.-4:30 p.m.

Symposium on Thyroid Function Tests and Diseases

Manchester Memorial Hospital

Speakers: Herbert Selenkow, M.D., Peter Bent Brigham Hospital; David Becker, M.D., New York Hospital; John Brooks, M.D., Peter Bent Brigham Hospital; Bruce Bower, M.D., Hartford Hospital

Program Chairman: Martin Duke, M.D., Department of Medical Education, Manchester Memorial Hospital (643-1141)

Registration Fee $2.00

April 24 9:30 a.m.-4:30 p.m.

Prevention of Cardiovascular Disease—What Is Known and What Is Needed

Mermaid Tavern, Stratford Motor Inn

Speakers: J. Gordon Barrow, M.D., Atlanta, Georgia; Alton Blakeslee, Science Writer

Sponsors: Connecticut Heart Association, Connecticut State Department of Health, Connecticut State Medical Society

Contact: Mrs. Schroeder Burnham, 103 Husted Lane, Greenwich (869-0670 or 756-8113)

Open to all physicians

May 16-18

Cardiovascular Symposium

St. Francis Hospital, Hartford

Speakers: Michael DeBakey, M.D.; Donald Effler, M.D.; C. Walton Lillehei, M.D.; Sidney Blumenthal, M.D.; Benedict Massell, M.D.;William B. Kannel, M.D.; Bernard Lown, M.D.

Contact: Robert M. Jeresaty, M.D., Director, Medical Division, Cardio-Pulmonary Section, St. Francis Hospital

PSYCHIATRY

February 6 1:30 p.m.

Forensic Psychiatry

Kettle Building, Norwich Hospital

Speaker: John Donnelly, Psychiatrist-in-Chief, Institute of Living

Sponsor: Connecticut Postgraduate Seminar

Contact: Vincenzo Cocilovo, M.D., Assistant Superintendent Norwich Hospital

Open to all physicians

February 14 1:30 p.m.

Personality Development and Psychopathology

Kettle Building, Norwich Hospital

Speaker: Maurice E. Linden, M.D., Director of Mental Health, Community Health Services, Philadelphia, Pa.

Sponsor: Connecticut Postgraduate Seminar

Contact: Dr. Cocilovo

Open to all physicians

CONTINUING MEDICAL EDUCATION

Yale University School of Medicine

Anatomy 201: Special Dissection in Anatomy
Course schedule and fee will be arranged

Anatomy 202: Demonstration in Anatomy
Course runs through May 28; fee $175

Epidemiology and Public Health 100: Introduction to Epidiomology
Designed for general practitioners. Course runs from February 20 to March 14. No fee.

Radiology 304: Clinical Laboratory Application of Radioisotopes
Course runs from February 29 to May 16.
Fee $150.

Institute of Living

Course in Psychiatry for Practicing Physicians
First 10-week course underway since November; second 10-week course begins in April. No fee.

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AMA-ERF

PROGRAM

What is AMA-ERF?

The American Medical Association Education and Research Foundation was established January 1, 1962, combining two previously established foundations. The American Education Foundation was established in 1951 for the purpose of providing financial assistance to medical schools. The American Medical Research Foundation, established in 1957, had as its principal aim the betterment of public health through scientific and medical research.

What are the purposes and programs for the Auxiliary?

To assist in raising funds for the three programs that we have chosen to support. These are:

1. Funds for medical schools—an unrestricted fund to be used to help pay faculty salaries; to buy modern laboratory equipment, library materials, and building improvements; and to provide emergency funds for student needs or other necessities of the school.
2. The loan guarantee fund—a fund that provides loans for students, interns and residents at low interest.
3. The Institute for Biomedical Research—helps pay salaries of senior scientists, laboratory assistants and technicians; helps buy laboratory equipment and supplies; and provides a free, unrestricted atmosphere where creative research on the nature of the cell and substance of life can flourish.

Why should I support the AMA-ERF?

Private support is an absolute necessity if medical education is to remain at its present high level. To help each new generation carry medical knowledge forward . . . to meet the need for more qualified physicians requires your help.

Research has become a most important part of modern medicine. Private support assures the scientist that he will be able to carry on his work with financial security. A continuous supply of funds is necessary for sophisticated in-depth research.

HEALTH CAREERS

In health career projects our primary concern is the recruitment of people of all ages to the health professions and occupations. Physicians are alarmed about the acute shortage of health manpower in hospitals, laboratories and nursing homes. Anyone who has been associated with health care facilities is keenly aware of the need for workers in all of the ancillary health professions.

In the past, auxiliary interest was focused on students from the 6th grade level on. To motivate them to select a future in the health field several successful projects have been used: health career days, health career clubs, programs on health careers in the schools, as well as programs for guidance counselors.

Recently it has been suggested that recruitment efforts be turned in the direction of adults. Help is sorely needed now and hospitals, laboratories and nursing homes cannot wait for lengthy training periods, after which they obtain inexperienced workers. We can direct efforts to adults confronted with the necessity of changing jobs, workers whose jobs have been automated or who wish to upgrade themselves, housewives whose family situations allow them to return to work, hospital volunteers (already motivated to help the sick) who might seek paid employment in a health career, and returning military personnel. Many auxiliary members trained in one of the health progressions have returned to work, at least on a part-time basis, to alleviate this critical situation. Projects for accomplishing this include: presentation of the "Health Career Package Program"; displays in booths at state, county and Health Fairs with auxiliary members to man them.

Woman's Auxiliary to the AMA
Member Orientation Manual

In Memoriam

Dennett, Roger H.—New Haven, New York University Medical School, 1949. Dr. Dennett was a practicing psychiatrist in New Haven for over ten years. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Dennett died December 21 at the age of 52.

Murphy, James J.—Danbury, Georgetown University School of Medicine, 1935. Dr. Murphy was a well-known general practitioner in Danbury for the past 30 years. Dr. Murphy was a former chief of medicine on the staff of Danbury Hospital, a director of the Connecticut Academy of General Practice, and was active in the American Academy of General Practice. He was formerly police surgeon and town physician for Danbury. He was a member of the Danbury Medical Society, the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was also a member of the American Geriatric Society. Dr. Murphy died November 27, at the age of 59.

Rademacher, Everett S.—New Haven, Iowa College of Medicine, 1923. Dr. Rademacher was a specialist in psychiatry in New Haven for over 20 years. He was on the staff of the Yale-New Haven Hospital. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was a Fellow of the American Orthopsychiatric Association. Dr. Rademacher died November 15, at the age of 68.

Stein, Julius D.—Fairfield, College of Physicians and Surgeons, Columbia University, 1944. Dr. Stein was a pediatrician in Fairfield for over 15 years. He was a member of the staff of St. Vincent's, Park City, and Bridgeport Hospitals. He served as a captain in the U.S. Army Medical Corps during World War II. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Association, and the American Medical Association. Dr. Stein died November 16, at the age of 46.

Around The State

Board Of Governors
New Haven County Medical Association
November 30, 1967

In spite of the very inclement weather the Board of Governors held a very well attended meeting at the Colonial House, Hamden, Conn., on Thursday, November 30, 1967. Twenty-three members were present. The business of the meeting was largely occupied with a report of the Review Committee. After hearing a presentation by the attending physician involved, the Review Committee's decision in two questions of "medical necessity" was reversed by the Board of Governors. Bills for the treatment in these two cases are to be paid as presented to the "Third Party."

In another case the Review Committee reported its success in compromising a bill for services rendered to the satisfaction of all concerned. The Clerk rendered an accounting of the finances involved in the very successful semi-annual meeting held in October, and a report on our Speaker Seminar which was sponsored by the A.M.A. and held on November 16th. He also announced the annual contribution to the Woman's Auxiliary Program prepared for the Annual Burgundy Ball.

An Ad Hoc Committee was appointed to review attendance delinquency of those members who have failed to comply with the By-Law provision. The meeting adjourned to the social hour and dinner which followed.

Respectfully,
H. A. Levin, M.D., *Clerk*

Action Programs
Urged For Poor

Development of high-quality health care for the poor through action programs based on community self-studies with the help of all agencies involved was urged by Irwin Miller, chairman of the Board, Cummins Engine Co., before the National Conference on Health Care for the Poor.

Reporting on the discussion groups held during the meeting, Miller, Conference chairman, said these studies are "the only intelligent base upon which new structures or organization, manpower, public education, and delivery mechanisms can logically be erected.

"No national model for such studies will suffice," he said. "The priorities are local or regional."

AME Suggests Guidelines For Professional Courtesy

Guidelines to help physicians resolve questions related to professional courtesy have been adopted recently by the Judicial Council of the AMA.

"The Judicial Council reaffirms and endorses the principle of professional courtesy as a noble tradition that is adaptable to the changing scene of medical practice," the council memo accompanying the guidelines says.

"Professional courtesy is not a rule of conduct that is to be enforced under threat of penalty of any kind," the Council continues. "It is the individual responsibility of the physician to determine for himself and within his own conscience to whom and the extent to which he shall allow a discount from his usual and customary fees for the professional services he renders, and to whom he shall render such services without charge as professional courtesy."

The guidelines:

- Where professional courtesy is offered by a physician but the recipient of services insists upon payment, the physician need not be embarrassed to accept a fee for his services.

- Professional courtesy is a tradition that applies solely to the relationship that exists among physicians. If a physician or his dependents have insurance providing benefits for medical or surgical care, a physician who renders such service may accept the insurance benefits without violating the traditional ethical practice of physicians caring for the medical needs of colleagues and their dependents without charge.

- In the situation where a physician is called to render services to other physicians or their immediate families with such frequency as to involve a significant proportion of his professional time, or in cases of long-term extended treatment, fees may be charged on an adjusted basis so as not to impose an unreasonable burden upon the physician rendering services.

- Professional courtesy should always be extended without qualification to the physician in financial hardship, and members of his immediate family who are dependent upon him.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

The Psychoanalytic Study Of Society. Volume IV. Edited by Warner Muensterberger and Sidney Axelrad. International Universities Press, Inc., New York, 1967. 350 pp.

Neuropsychiatry In World War II, Volume I. Editor in Chief, Colonel Robert S. Anderson, MC, USA; Editors for Neuropsychiatry, Colonel Albert J. Glass, MC, USA (Ret.) and Lieutenant Colonel Robert J. Bernucci, MC, USA (Ret.). Office of the Surgeon General, Department of the Army, Washington, D.C., 1966. 826 pp. with 65 illustrations, 16 charts, 67 tables. $7.50.

Ocular Therapy, Complications and Management. Volume II. Edited by Irving H. Leopold, M.D. The C. V. Mosby Company, Saint Louis, 1967. 139 pp. Illustrated. $11.00.

Atlas Of Strabismus. Edited by Gunter K. von Noorden, M.D. and A. Edward Maumenee, M.D. The C. V. Mosby Company, Saint Louis, 1967. 115 illustrations, 29 in color by Robert B. Wingate, M.S., F.R.S.A., 188 pp. $17.50.

Conference on Micro-Vascular Surgery. Edited by R. M. Peardon Donaghy, M.D. and M. Gazi Yasargil, M.D. The C. V. Mosby Company, Saint Louis, 1967. 217 illustration, 171 pp. $17.50.

Comprehensive Textbook of Psychiatry. Edited by Alfred M. Freedman, M.D., Harold I. Kaplan, M.D. and Helen S. Kaplan, M.D., Ph.D., Assistant to the Editors. The Williams & Wilkins Company, Baltimore, 1967. 1666 pp. $24.75.

Evolutionary Biology, Volume I. Edited by Theodosius Dobzhansky, Max K. Hecht, and William C. Steere. Appleton-Century-Crofts, New York, 1967. Division of Meredith Publishing Company. 444 pp.

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BOOK REVIEW

ENDOCRINOLOGY OF THE TESTS: CIBA FOUNDATION COLLOQUIA ON ENDOCRINOLOGY, Volume XVI. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, Massachusetts 02106, 1967, 331 pp., 93 illustrations. $12.50.

Reviewed by: MARVIN HARVARD, JR.

Publication of the proceedings of this colloquim represents an awakening concern about the many aspects of male endocrinology. The fifteen papers presented before twenty-six internationally prominent investigators in this field present a broad spectrum of current investigations as well as newer techniques of study and clinical application which are richly augmented by free and candid discussion fully reported. The volume is not one for the uninitiated. A broad background, particularly in biochemistry, embryology and genetics, is needed to savor it fully. Its emphasis, endocrinologically, is upon the possible direct effects of testicular hormones, especially testosterone, upon spermatogenesis.

Of interest to clinicians will be a paper on "Testicular Function in Man" in which the normal endocrine function of the testis and its contribution to androgen secretion is discussed along with certain aspects of androgen deficiency manifested by loss of libido and potentia. Most striking is a study of 29 previously potent males without other manifestations of androgen deficiency. In all but two of these testosterone levels were within the normal range and the mean level in the group did not differ significantly from that of the normal population, thus providing objective evidence that the symptoms are most probably of psychogenic origin. Further support to this view was given when, in the two patients with low testosterone levels, with environmental adjustment and psychotherapy their levels rose to near normal and the symptoms were ameliorated.

Of further interest to clinicians is the description of a new syndrome called "mixed testicular dysgenesis" because histological study of the testes shows a mixture of two or more of the patterns observed in Klinefelter's syndrome and in the syndrome of alteration in spermatogenesis. Eight cases are described. Phenotypically they are heterogeneous, but all had hypoplastic testes and a small penis with increased urinary gonadotropin excretion in all save one.

Excellent references.

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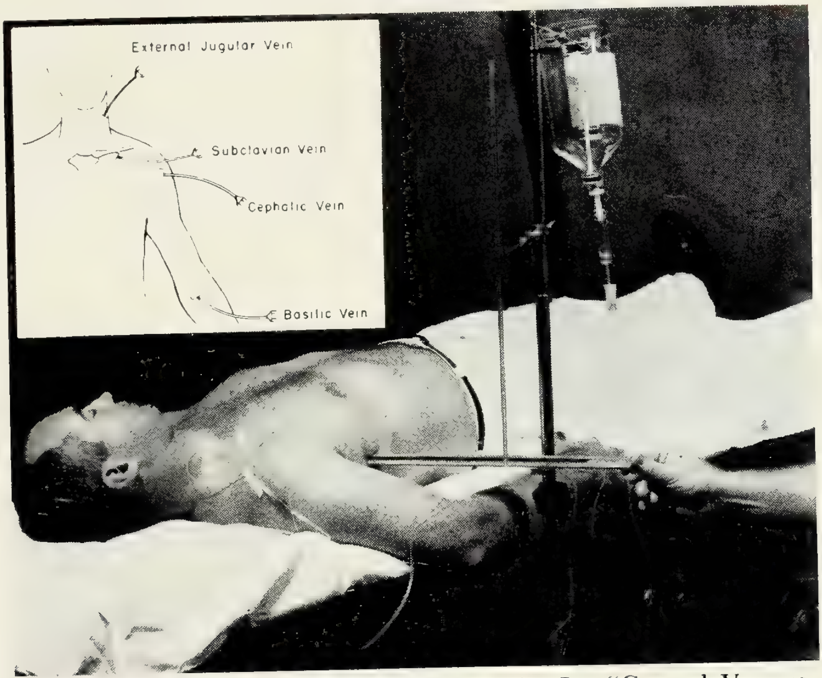

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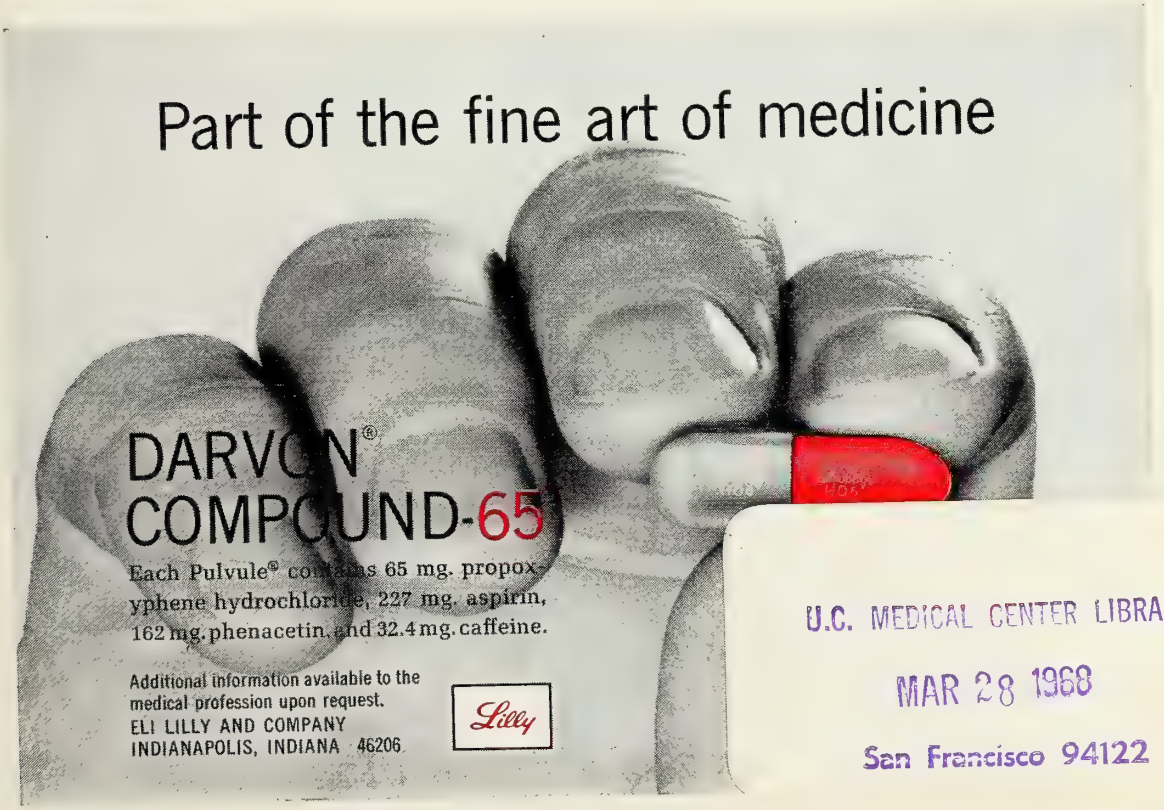
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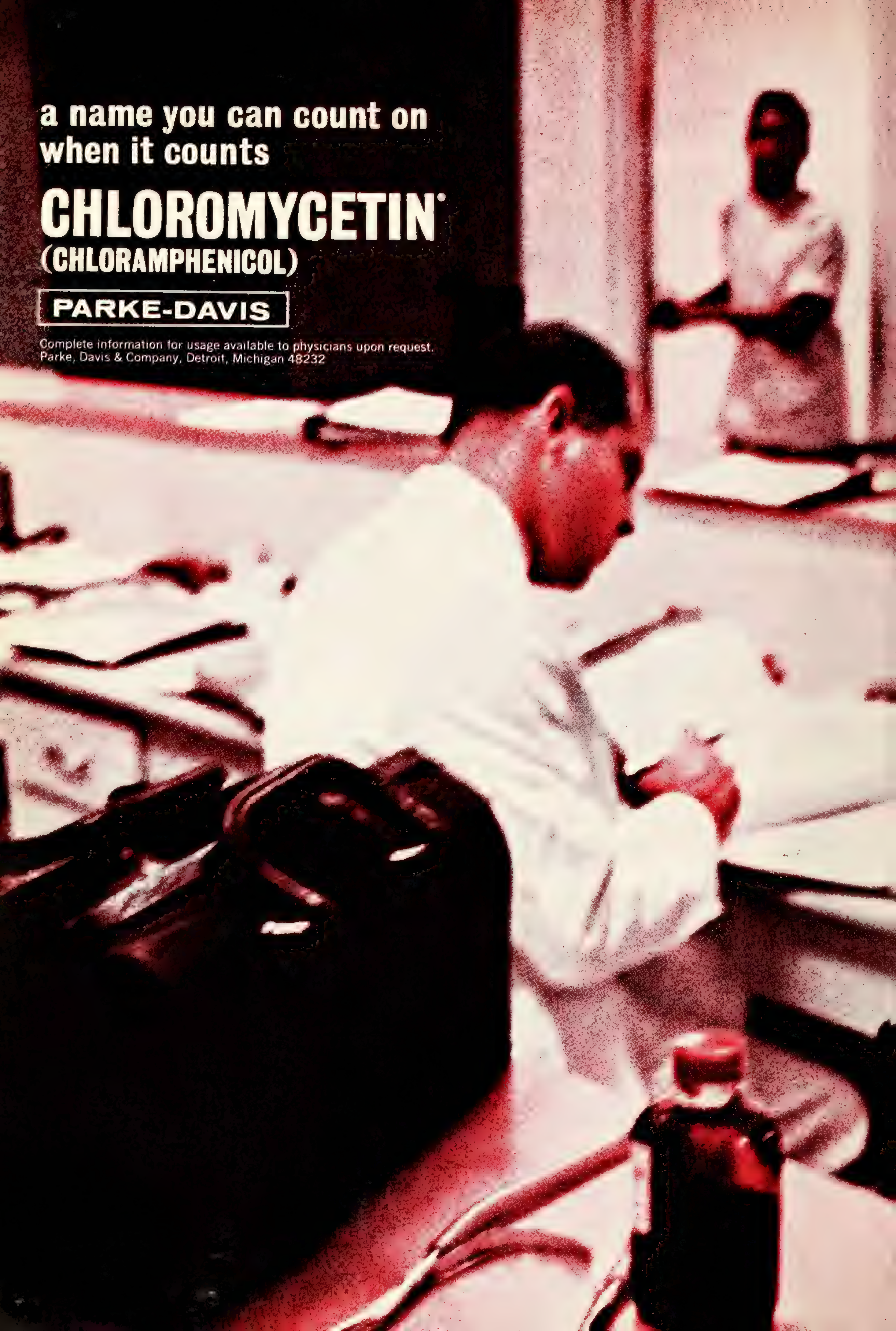

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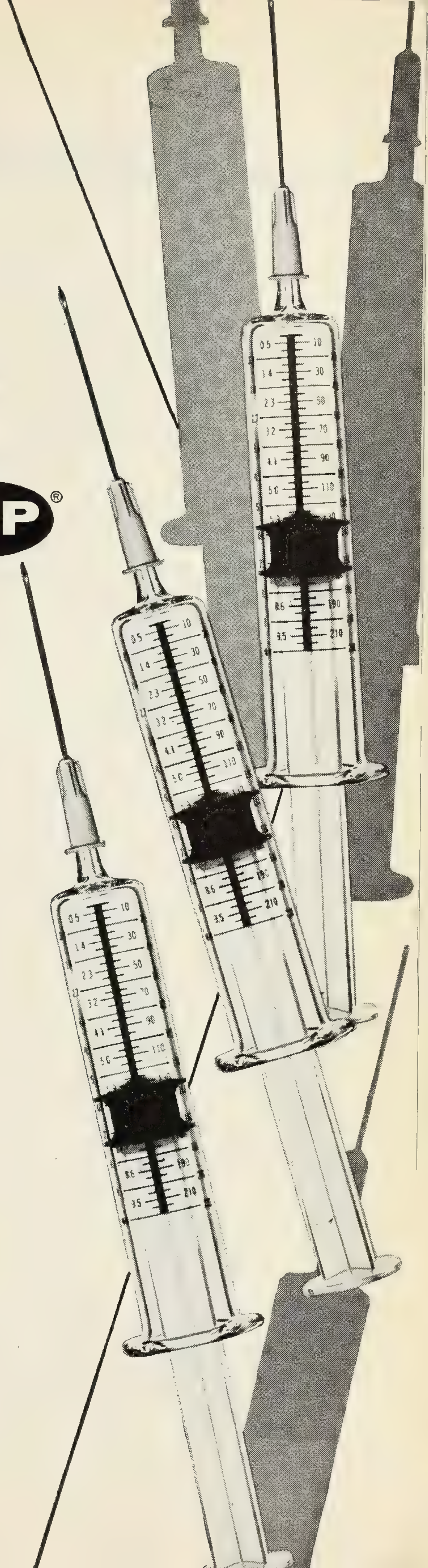

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Connecticut Medicine

editorials

Central Venous Monitoring In Shock

In shock we find three possible hemodynamic abnormalities, cardiac failure, circulatory volume deficit and peripheral vascular failure. It isn't always easy clinically to assess the hemodynamic abnormality that is operating. By measuring the central venous pressure (CVP) and its response to rapid trial infusions we do possess an excellent method of determining the abnormality that exists. The CVP is the venous pressure as measured in the great veins within the thorax. The technic described by Eastridge and Hughes (see front cover) is to insert a small polyvinyl catheter into the median basilic or cephalic or subclavian vein by percutaneous puncture or if needed by cutdown. With a three way stop cock attached to the catheter one can record venous pressure from a zero reference point found in the midaxillary line.

The catheter should be changed every three to five days to avoid the complications such as thrombosis, embolism, suppurative thrombophlebitis, sepsis and chemical necrosis resulting from infusion or irritant solutions. The operator should, of course, first gain experience on a cadaver, to become familiar with the principal anatomic relations of the subclavian vein and to discover the best course for the needle to follow during insertion. In this way septicemia and thrombosis is avoided. So is perforation of the vein by the catheter tip, catheter embolization or fragmentation or division of the catheter by never withdrawing the catheter through the needle while it is in the vein.

The level of the CVP is the result chiefly of a complex interaction of the pumping action of the heart, the blood volume and vascular tone. Normally the heart controls the outflow from the venous system. A deficit in cardiac contractility will lead to piling up of blood in the venous reservoir and increase CVP. The blood volume, however, and vascular dynamics must remain stable. If the heart remains normal then the CVP will decline if blood volume declines or if the peripheral vasodilation causes pooling in the microcirculation with reduction in venous return.

The cardiac defects encountered in shock are many, primary heart failure as seen in elderly people with previous heart disease. A failure of metabolic support in a normal heart could take place from hypoxia, metabolic or respiratory acidosis, derangement of serum electrolytes, especially sodium and potassium. Heart failure may be precipitated by an intensified peripheral resistance from circulating catecholamines and direct effect of toxins on the myocardium. Other factors that may cause the heart to fail as a pump are arrhythmias, tamponade, tension pneumothorax. A most serious one is, of course, acute myocardial infarction.

In shock associated with an initial vasoconstriction as encountered in untreated hypovolemia, cardiogenic or gram-negative septic shock, the venous return is greatly reduced, the CVP is low. Then acidosis, anoxia develop and lead to loss of arteriolar sphincter tone but venous sphincter tone may persist. Blood will then enter the capillary bed but can't leave it. As a result capillary hydrostatic pressure exceeds colloid osmatic pressure forcing intravenous fluids into the extravascular space and cause irreparable tissue damage and loss of circulatory blood volume.[2]

Accordingly when we are presented with a patient in shock we must be concerned with the clinical cause of the state of shock as well as the hemodynamic abnormality present. A patient can be saved by prompt shock treatment based on hemodynamic abnormality alone. This can be

THE COVER

Figure 2. Sites for percutaneous puncture or insertion by "surgical cutdown" of intracaths or polyvinyl catheters for monitoring the central venous pressure used in treating shock.

Figure 3. Water monometer in the intravenous system for monitoring central venous pressure and the method of determination of the "zero reference points" on the patient and manometer.

quickly determined by inserting an intravenous catheter into the superior vena cava to monitor the CVA. The catheter can also be used as an avenue for fluid trial infusions of 300–500 cc. If a patient is in shock and his CVP is low (6 cm. or less of water) then rapid infusion of suitable volume-expanding solutions may be administered safely until the circulatory dynamics become stable or the CVP rises to 8–12 cm. of water. If a volume defect is the hemodynamic abnormality, the arterial pressure will respond quickly to rapid volume replacement and urine will usually return.

If an effective circulating volume has been restored in a patient in shock with the CVP 8–12 cm. of water and he remains in shock or if the patient has a high CVP when first seen the primary problem is cardiac. Then the acidosis which is present in most patients is corrected by sodium bicarbonate, the cardiac contractility must be improved by instilling 1–2 mg. isoproterenol in 500 cc. dextrose in water intravenously, regulating the flow so that normotension and adequate cardiac output are maintained at a heart rate of 110 or less per minute. Digitalis is usually also indicated but the heart response will be less rapid.

If the patient remains refractory to this therapy and his blood pressure fails to respond, Callaghan and Watkins urge consideration for the use of arterio-arterial counterpulsation. They point out that if a patient has cool moist skin, a thready pulse the CVP and arterial pressure is low, volume expansion must first be tried and only if arterial pressure fails to rise, should counterpulsation be undertaken. In the patient with warm skin, slow pulse who fails to respond to conventional therapy, then counterpulsation will have its best effect. It might lead to rise in arterial pressure, better coronary perfusion and lowered myocardial work and save a life of an otherwise hopeless patient.

Once the circulation is restored it becomes necessary to consider the possible clinical causes of cardiac dysfunction and institute appropriate therapeutic measures if possible. A transient and unsustained response to the CVP and arterial pressure after large rapid volume replacement suggests peripheral vascular failure due to peripheral pooling. Eastridge recommends large doses of hydrocortisone (2 grams over a period of a few minutes). Additional volume expanding fluids may then be necessary because hydrocortisone reduces peripheral resistance, increases the size of the vascular bed and this requires larger amounts of fluid.

Eastridge prefers lactate Ringer's for rapid infusion in shock not due to massive loss of red blood cells. This type of solution serves to reconstitute the sodium space which is reduced in shock. However, the primary determinant of an adequate circulating blood volume are the red cell mass as well as the rapidly exchangeable sodium salts of the body and in hemorrhagic shock with massive loss of red cell mass a combination of buffered saline and sufficient blood to maintain adequate oxygen transport is required rapidly.

Monitoring CVP then turns out to be invaluable in promptly assessing the hemodynamic abnormality causing the state of shock and leads to its rapid correction. The level of CVP at any single measurement is often less significant than the response of the CVP to rapid trial infusions. In general patients in shock with a low CVP have either a volume deficit, more rarely peripheral pooling. If the CVP is elevated or rising this indicates myocardial insufficiency and improving myocardial function becomes the major task. Failure in this regard requires consideration for use of arterio-arterial counterpulsation.

L.H.N.

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Elements Of A Psychologic Examination

When we are confronted with a multitude of obscure human problems with no firm guidelines between the normal and abnormal we must become more proficient in the principal elements of a psychologic examination. We need to look closely at the patient's appearance and behavior, his mood, his mental control, his insight and judgment and also his capacity to feel. If we become proficient we will readily identify significant symptoms and signs which can lead to a firm diagnostic appraisal.

The psychologic examination has gone through several evolutionary stages. In the 19th century emphasis was placed on objective phenomena particularly motor such as catatonic signs. Histories were sketchy and social environment not routinely investigated. In the modern period psychiatric interests and methods strike behind symptoms and signs to pathologic processes: in schizophrenia processes involved in splitting the personality, in psychoanalysis, a host of special mechanisms such as repression, projection reaction formation, importance of denial and many others. Psychiatrists and psychologists began to collect in great detail the patient's account of his subjective experiences, the sense of time, space, color, an attempt to obtain knowledge of pathologic psychic life from within.

There has grown up also the systematic investigation of social, institutional and family contributions to disturbed mental life. The methods include all the technics of psychiatry but applied beyond the patient to his surrounding figures. The epidemiology and ecology of mental illness, family dynamics, the impact of hospital life on patients, in short the sociology of psychiatry, the "environmental envelope" of psychic life, the conditions and interactions that shape individual psychologies from without. The modern psychiatrist is obliged to understand his patient's family, class and social experiences as a modern internist is to know his patient's dietary habits and environmental hazards.

In the psychologic examination the patient offers us a specimen of his social interactions. He will, within certain limits, treat the physician as he does many others in his environment. In addition the physician's reaction to him should give important clues as the way in which others feel about and treat him. This of course is within certain limits, since he will not treat us just as he does everyone else and our reactions will not be exactly that of many others. But for all our "specialness" as individuals and as doctors, the patients treatment of us and our reactions to him can provide leads to much that is occurring elsewhere in his life.

Physicians must keep as careful track of their responses to the patient as they do of his to them. Does the patient look depressed? He may not, in fact, he may state that he is happy and content. We may, however, sense in our own mood in his presence a little despair, a little turning away. Our mood may be other than the patients. Perhaps it is late in the afternoon, or we are running behind our appointments, but perhaps it is not of these things. Feelings are categories. The clues of our own response may be the only clue to depression, and should be enough to energize the search in other areas, and to review more carefully the recent experience, the state of his relationships or disappointments in life's work. We may not be sure, but it means there are other things to do. The point is that the physician has as an instrument in himself with which to sense concealed despair in his patient.

Finally psychiatry has been enormously enriched by the free association method of psychoanalysis. Mental content that comes to light relatively free of self-editing social conventions and censorships of many kinds has provided connecting links that make intelligible a great body of material hitherto obscure. The impact of this on the psychologic examination has been immense. Medicine has learned the value of listening more and talking less, of concentrating attention on lapses, puzzling details, jumps of logic, dreams, slips and jokes, misunderstandings of all kinds, any of which may lead to underlying themes, ideas and aspirations of the greatest importance. There is great value of listening with a third ear. The tracking down of physical disease has always required the finest sensitivity and intuition, the willingness to follow up what seems hardly present at all, an openness of mind not only to the loud and obvious but to the obscure and apparently insignificant as well.

Thus we see that an adequate psychologic examination requires that the patient be observed as always, his speech, expression, movement, dress, the fullest range of outer signs. It also requires that we learn as much as possible of the "inner experience" of the patient admittedly one of the most difficult depths to plumb. The examination further demands self-examination, how the patient makes us feel, what personal responses on the one hand reflect the patient's mood and on the other, undermine through contagious sadness or annoyance, the physician's most complete and objective professional attention. Through all this we must listen for anything that does not fit or for things that fit too well.

While still conducting the examination we must compare the information being obtained from the various sources and decide what psychological processes are at work. We may note for instance that the patient shuts out every unpleasant topic just as he approaches it and replaces the unpleasantness with something cheerful and therefore misleading. This smiling on the outside while crying on the inside is called the "manic defense." We then have to press a little to see how sturdy is the defense and what lies behind it.

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Physiology And Medicine: Exercise In Intermittent Claudication

What can the physician offer his patient for relief or improvement of intermittent claudication besides surgery which is rarely applicable anyway. Limb survival with arterial occlusion is possible because the collaterial arteries bypass the obstruction. However, the bypassing arteries are narrow high resistance pathways and therefore offer reduced capacity to deliver blood to the exercising muscles. Several vasodilator drugs are available and are used but their efficacy is open to question. There are also clinical observations on the use of exercise to stimulate collateral development. Some patients report that they can walk farther after recovery from the pain of claudication brought on by an initial walk. This is a subjective test. It brings to mind similar experiences of some patients who "walk through angina" and can then continue their exercise without further pain.

Skinner and Strandness[1] have reported their studies on effect of exercise on intermittent claudication. As an objective test of the efficacy of exercise they measured the arterial pressure at the ankle before and after exercise. We know that the magnitude of fall in pressure at the ankle reflects the extent of ischemia and the amount of time it takes for the arterial pressure to return to pre-exercise level reflects the degree of post-exercise hyperemia of the muscles. Thus it is possible to study improvement in claudication because improvement is accompanied by a lower reduction in arterial pressure at the ankle after exercise and a faster recovery. This test is a pre-requisite for devising a worthwhile program to evaluate effects of physical training after exercise.

As might be expected they found marked differences in subjects. All had after repeated exercise an effect on arterial pressure response. If repeated exercise of sufficient intensity is undertaken then progressive vasodilatation does occur. Repeated stimulus for increased blood flow has a training effect. The patients were able to walk longer. They got their pain later in the walk and there was an increase in resting arterial pressure level at the ankle. The question arises what would happen over an extended period of graded exercise to legs that suffer from intermittent claudication.

Skinner and Strandness studied effect of training five patients over a three to eight months period of supervised individualized exercise to determine the role of exercise as a therapeutic method in the

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treatment of intermittent claudication. Three subjects showed significant increases in resting arterial pressure levels at the ankle even though there was no increase in arterial pressure in the arm. Clearly this indicated a reduction in the pressure gradient across the collateral vessels and increased blood flow to the ischemic muscles.

Training also showed a significant increase in the time of onset of claudication and in the maximum time the patients could walk without pain. A reduction in pain while walking also occurred the so-called "walk through" phenomenon which has also been reported in angina pectoris and also reflects vasodilation of collateral arteries. All five subjects showed gratifying increase in arterial pressure at the ankles two minutes after exercise and this indicates a reduction in the amount of ischemia and a greater capacity of the collateral vessels.

The data presented appears to have a single interpretation, namely that physical training is feasible and has a beneficial effect in some patients with arteriosclerosis obliterans. The improvement is the result of improved collateral circulation to the obstructed leg at rest, during exercise and during the recovery period. Buerger's old view that one can develop a collateral circulation by passive movement was not confirmed by Skinner. On the contrary, postural movement caused no change whereas increased flow occurred in men during or shortly after exercise and was definitely related to the intensity of the exercise. Similar results have been reported by Lassen[2] and others.[3, 5]

One question relates to the amount of exercise one should encourage the patient with intermittent claudication to undertake. Apparently there is little effect of repetition of exercise on the arterial pressure in the ankle if work intensity did not exceed claudication pain time. However, a higher work load is known to result in a greater post-exercise hyperemia of muscles. Within limits it is theoretically logical to assume that the greater the ischemia, the greater is the demand for blood and the greater is the need for adaptation by blood vessels. From the standpoint of therapeutics we must train our patients by administering enough exercise to induce the pain of intermittent claudication, since this is the most rewarding in terms of increasing collateral circulation.

The principle of training to improve the circulation of muscles has also been applied in the case of the coronary circulation. Zoll et al[6] observed increases in coronary collateral circulation which was proportional to the degree of arterial obstruction. Eckstein[7] found this to be the case and also that there was no increased collateral circulation with mild coronary constriction unless exercise was added. The exercise promoted a greater vascularity in dogs with moderate or severe constriction than it did in control dogs who were not exercised.

There is suggestive evidence in the literature that increased physical activity has a beneficial effect on the course and severity of coronary artery disease.[8, 9] And so we see that the therapeutic use of exercise is derived from a well known physiological mechanism termed "auto regulation" in which local vessels are caused to dilate by CO$_2$, metabolites and bradykinin released during activity.[10]

L.H.N.

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Experiments in Postgraduate Education: Setting The Learning Process In Motion By The Medical Audit

The medical audit is the only situation in the practice of medicine which provides an element of compulsion for continued learning.[1] The compulsion, however, is quite palatable by being imperceptible. Most physicians practice in a hospital setting. It is hospital practice which offers an available medium for establishing and assessing professional standards in medicine. The physician documents on the chart the care he gives his own patient and a systematic analysis of the competence employed in treating a patient is highly superior to any surveillance possible by a medical society or a state licensing board. There is also very little doubt that the quality and standard of care rendered in a hospital does carry over into the physician's outside practice.

Any opportunity for the physician to learn from his errors and shortcomings will make him do better in the future and analysis of his cases in the hospital must offer an opportunity for physicians to grow in knowledge, judgment and skill. When cases are audited in the hospital setting the physician will not continue to repeat the same experience many times as soon as he learns that this experience is inferior when measured against realistic progressive standards.

The concept of the medical audit is being rightly advanced as educational and not control, discipline or regulation of the physician. It is not, as some fearfully believe, a plan to regiment practice of medicine, to beat down the general practitioners or "to give the boys who are in an excuse to cut my privileges". In recent years Eiselle[2] assures us that he has encountered no instance in which such tactics have had any notable success, certainly not for long.

The concept underlying the medical audit go back to the very beginning of our profession. Ours is a learned profession, unselfishly dedicated to the welfare of his fellow man. High in the test of this philosophy is the physicians willingness to engage in self-evaluation, self-criticism and self-discipline. The opportunty for self-evaluation is easily available to our profession in the hospital patients clinical record which becomes a tool for professional self-appraisal and self-discipline.

The educational aspects of a well conducted medical audit answers many of the major criticisms of traditional continuing education surprisingly well. Medical educators would do well to explore the uses of this new tool. Until now they have failed to appreciate its significance and usefulness. It satisfied the special educational needs of the practicing physician in a variety of ways.

The first is that the educational benefits of a medical audit are universally available wherever there is a hospital, small or large, remote or near medical centers. The only limiting factor is motivation of the medical staff. There are 800 hospitals across the country who have the audit in operation. One rural hospital with less than 100 beds has had an active medical audit committee since 1950 and all members of the staff work on the committee in rotation.

The medical audit utilizes the highly esteemed self-education principle, which is becoming the ultimate goal of all formal education. The physician is stimulated to seek knowledge on his own initiative. Assuming the physician wants to learn, the medical audit helps him find out how he can do this. All members of the staff are involved and those who serve on the audit committee reap the greatest educational benefits. It is for this reason that it is wise for all members of the staff to serve on the committees in rotation. The review of the medical audit results with the staff in an additional learning experience. The reluctant physician who shuns postgraduate courses avoids scientific meetings in his hospital or county society will not be able to escape the impact of the medical audit on his and the staff's patients.

Learning proceeds best and retention is greatest when the student is an active participant. The medical audit uses the physicians own patients and his own experience. In this way the physician is motivated to engage in formal as well as informal

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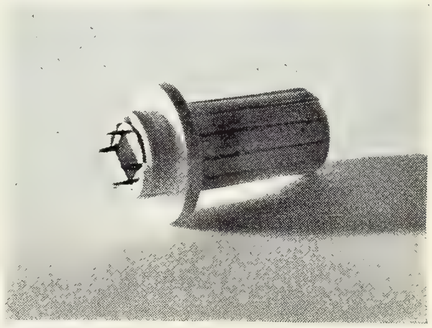

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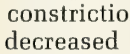

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continuing education. When being faced with ones own errors and deficiencies is the most effective way of making the doctor hustle to the library. The motivation to excell is especially great when one sees ones record compared objectively with those of his fellow staff members and especially when anonymous interhospital comparisons show that his own mediocre work caused his hospital staff to suffer by comparison. Once the physician begins to revisit the library and the learning process is again set in motion it is an easy step for him to seek more formal instruction.

The medical audit more than most other educational processes achieves the ultimate goal of continuing education, the improvement in the quality of patient care. It seems to have been the common experience of hospitals of all types and all sizes that when a well motivated and a well conducted medical audit program is introduced, the standards of care are elevated and conformity to the standards are improved. These desirable effects are more noticable if the motivation for the medical audit is education not control.

L.H.N.

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The Thyroid Nodule

Any thyroid nodule which secretes thyroid hormone without control from the thyroid stimulating hormone (TSH) arising in the anterior pituitary, is considered to be autonomous. There appears to be several types of nodules which are characterized by the amount of 131[1] which they concentrate as determined by the thyroid scanning technique. If the nodule concentrates iodine to the same extent as the extra nodular portion of the gland, it is termed "warm" and considered TSH dependent. It is termed "hot" and hyperfunctioning if it concentrates radioiodine to a greater extent than the surrounding thyroid tissue. These nodules secrete enough thyroid hormone, this may lead to complete suppression of TSH production and in consequence, the function of the remaining extranodular thyroid tissue will be suppressed.

Many patients with such nodules will remain euthyroid if the autonomous nodule does not secrete enough hormone to produce hyperthyroidism. There are, however, some such nodules which do secrete excess of thyroid hormone and produce hyperthyroidism. These "hot" nodules may be TSH dependent or autonomous. McCormack[2] demonstrated autonomy in fifteen hyperfunctioning nodules. Not all nodules, however, are autonomous. Some are pituitary dependent because their 131[1] uptake can be suppressed and their size diminished by administration of thyroxine.

There appears to be no reported data as to whether these nodules once having escaped pituitary control remain permanently autonomous or whether they may once again become responsive to endogenous TSH. Up to the present time the vast majority of these patients have been treated either surgically or with radioiodine. Obviously if some of the nodules were to go back to pituitary control, then we might rethink our practice of treating them. But then we would seek for clues in these patients as to which ones would lose their autonomy and which ones might develop hyperthyroidism.

Silverstein et al[1] studied the natural history of a group of patients with autonomous hyperfunctioning thyroid nodules in order to resolve this question. They studied nine patients over a period of two to seven years. None developed hyperthyroidism during the period of observation. Moreover, the data they obtained indicate considerable variability in the natural history of the autonomous hyperfunctioning thyroid nodule. Four of the patients had persistence of autonomy but varied in the amount of thyroid hormone they produced. Three had reestablishment of TSH dependence. One patient developed degeneration within the autonomous nodule. And one showed a reestablishment of normal pituitary-thyroid control.

One of the basic questions regarding the clinical manifestations of the autonomous hyperfunctioning thyroid nodule is the frequency of associated thyrotoxicosis. The incidence of hyperthyroidism in the reported series of hyperfunctioning thyroid nodule ranges from 33 to 100 per cent. It is interesting that the patient must also show the clinical signs and symptoms of thyrotoxicosis to be sure that the laboratory tests are accurate. This point cannot be overemphasized because of the tendency of some physicians to abrogate their clinical judgment and rely too much upon a laboratory diagnosis.

Another interesting question is whether a nontoxic hyperfunctioning thyroid nodule can eventually give rise to thyrotoxicosis. Silverstein points out that the preponderant course appears to be that in which autonomy persists without development of hyperthyroidism. He found but one of twenty-two patients with autonomous hyperfunctioning thyroid nodule during a follow up period ranging over seven years. Furthermore, there was no apparent correlation between nodule size and either the clinical course or the ultimate fate of the nodule. If and when a hyperfunctioning nodule does become autonomous, then its functional evolution could depend upon the relative balance between the process of hyperplasia and involution.

The two significant findings in Silverstein's series —variability in the natural history of the autonnomous hyperfunctioning thyroid nodule and also the prevalence of long standing euthyroidism, indicate that the mere documentation of the presence of such a nodule is not per se an indication for its immediate removal. Restoration of normally functioning pituitary thyroid control is certainly a worthy objective. But we will need long term follow-up of an increasing number of these untreated patients before we will have acquired further insight into the genesis and evolution of these nodules as well as their relationship to various aspects of thyroid dysfunction.

L.H.N.

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Sexual Ateliosis: A Primary Growth Hormone Deficiency

If a dwarf or midget is normally proportioned, he has been termed ateliotic by Gilford. If their sexual development and function is also normal they are then termed sexual ateliotics. The first question that comes to mind is why should anyone be interested in such individuals since they are so seldom encountered. The answer of course is that not infrequently a study of a rare disorder reveals to us the workings of fundamental laws of nature which are difficult to understand unless an individual is found in whom the law is deranged in some way. And so we must pay attention to the rare forms of disease or disorders to seek clarification for normal workings in the human body.

Rimoin, Merimec and McKusick had occasion to study six sexually mature indivduals with proportionate dwarfism in ages ranging from 39-77 years. Their weights varied from 66 to 100 pounds and their heights from 49-56 inches. None had any congenital malformation. Three were members of an inbred West Virginia kindred and three were husband, wife and a daughter. At birth their bone age and weight were normal. Accordingly the daughter had to be delivered by cesarean section. The growth retardation was first noted in the first two years of life. Five of the six grew gradually with a halt in growth after puberty which was delayed by 2-10 years. However, the secondary sex characteristics were normal. The skin was smooth, wrinkled, abnormally thick. Voices were high pitched with a small timbre.

All were in good health, none had hypoglycemia. What could have been the defect. If it was due to panhypopituitarism then they should have shown deficiencies of adrenal cortical function. They were however normal. They should also have shown hypogonadism but their sexual development was normal. If it was due to growth hormone deficiency alone, then these patients should have shown two things; a low level of growth hormone in the blood, and failure to show an increase in growth hormone in the blood after insulin administration. But for this a specific method for assaying growth hormone in the blood would be necessary.

Without such a method of assaying the blood for its growth hormone content neither of the two observations noted above could be made and former investigators recognized that sexual ateliotics were not caused by panhypopituitarism but were forced to relegate these cases to an "idiopathic" group, called them "primordial dwarfs" the tacit implication being that the defect is not pituitary, but is a genetically determined one at the "cellular level."

Once a method was discovered to assay blood for growth hormone, Rimoin, et al found all their six patients showed a deficiency of it and after administering insulin the growth hormone did not rise although in normal patients it rises ten fold. These normally proportioned, sexually mature midgets therefore were shown to have a deficiency of human growth hormone. Such a deficiency may be similar to that associated with inherited pituitary dwarfism in mice.

The authors found that puberty was often delayed in their patients and it may be that gonadotrophin formation though associated with growth hormone for a time, finally breaks through to result in normal sexual function in the absence of growth hormone.

Apparently sexual ateliotic dwarfism is inherited as an autosomal recessive trait. It therefore appears in siblings from consanguineous marriages but the mating of the two affected persons resulted in the birth of two similarly affected offspring. One of the affected offspring died accidentally in childhood but monotropic growth hormone deficiency was demonstrated in the two parents and the remaining daughter.

All of the six dwarfs studied had normal birth weights. Since the parents were deficient in growth hormone and the child also was years later, it raises the question as to whether growth hormone is required for intrauterine growth. We do not of course know whether growth hormone is manufactured by the fetus only to disappear after two years of life. Not only were the pregnancies normal and the fetuses were of normal weight at birth, but lactation was also normal and this clearly indicates that the growth hormone molecule (or at least those parts of it which are immunologically active and are involved in growth promotion), is not essential to postpartum lactation. Apparently it is in some way related to development of normal skin and normal voice.

If a mutation resulting in isolated deficiency of growth hormone occurs perhaps we will find, if we search for it, isolated deficiencies in man of pituitary gonadotrophin, adrenocorticotrophin or thyrotrophin.

Many additional questions arise. What would be the clinical picture of growth hormone, reduced by slow exhaustion, insufficient production or perhaps increased antagonism to it from some as yet unknown mechanism. Parahormone has its thyrocalcitonin, insulin, its glucagon. What is the antagonist to growth hormone. Is it insulin or another as yet unknown hormone. Clearly the clinical and other investigations of hereditary disorders must shed light on normal developmental and biochemical mechanisms.

L.H.N.

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Hemotherapy Now And In The Future: (Concluded)

The use of whole blood in certain practices has probably reached its peak during the last few years. On the other hand the utilization of blood components is lagging behind their present availability and known indications. It is altogether likely that their use will be progressively increased and that at the same time the use of whole blood will be actually decreased. The production of most of the whole blood components, however, will become more and more complicated and will consequently be limited to large centers. The average hospital blood bank will serve to an increasing degree as a collection station and depository.

Plasma maintains its place as a useful agent in certain situations but only too frequently hepatitis remains an ever present menace and although the danger can be reduced to some extent, the final solution is not likely to come before the virus of hepatitis is identified and isolated. The amount of plasma that could be made available is very great. In a recent report from Massachusetts there were 180,000 blood transfusions given in 1964. If all patients who did not need plasma had been given packed red cells 40–50,000 units of plasma would have been available for whole use or for preparation of plasma components.

Plasma components have their place in the therapy of certain conditions with promising results. With the use of cryobiologic methods, anti-hemophilic globulin has been made available and more recently hemolytic disease of the newborn has come under control with use of a gamma globulin fraction to produce passive immunity in an Rh-negative mother. All attempts thus far to prepare albumin and other plasma proteins from animals, mainly cattle, have led to no clinical usefulness because of antigenicity.

In the discussion of blood and blood components, one cannot exclude plasma expanders. These are functionally related to plasma and include such substances as providone (polyvinylpyrrolidone), dextran and levulan. There have been many studies of the first two, especially dextran. Dextran reduced blood and plasma viscosity and improved the circulation in small vessels.[2, 3] Until recently blood has been considered the ideal replacement therapy for hemorrhagic shock. Recent studies, however, suggest that low viscosity dextran may be more effective in controlling hemorrhagic shock than whole blood transfusions. In fact cases

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are on record in which improvement was noted from dextran after whole blood itself was ineffective. Such observations open up a whole field for plasma expanders as not just substitutes for whole blood or plasma. Dextran has also been recommended for thrombophlebitis and most recently for the treatment of purpura fulminans.[3]

In any discussion of hemotherapy the specter of hepatitis is ever present. Published reports of its incidence are unreliable partly because complete reliable follow up is extremely difficult. At the present time the best available means of reducing the incidence of the disease is adhering to established rules in the selection of donors. We are not yet sure of the reported favorable effects of gammaglobulin. A serious drawback is its limited supply. It may be that smaller doses may provide passive immunity and then favor the development of active immunity. In a recently carefully controlled study with 95 per cent follow up, patients undergoing heart surgery were not protected by a prophylactic dose of 10 ml. of gammaglobulin immediately before the operation and again thirty days later.

Some of the prognostications about the future of hemology are already close enough to be realized in the near future such as the further practical application of advances in cryobiology and the preservation of one's own blood and marrow for indefinite periods. Some of the others are somewhat further away. Here belong the growth in vitro of strains of one's own marrow cells and their use as autotransplants in the depositor. These, however, are far from fantasies. Their vague outlines can be seen forming on the horizon of medical research. The main thing that is needed to hasten their realization is to encourage pursuit of research by providing the necessary means and climate, both of them free of interruptions of any kind.

Who knows but that advances in cryobiology will spillover into many other areas: preservation of tissues and organs. Preservation of sperm cells for future use in the active pursuit of eugenics. Many other uses will surely come to view as the science progresses. For it is generally acknowledged that advances in one field always favorably affect advances in others.

L.H.N.

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The Physician And The Law. I. Pretrial, Trial And Post-trial

Each year many psychiatrists and other physicians are called by courts to render expert opinion regarding an individual's mental competency to stand trial. It is important that the physicians thoroughly comprehend the procedures involved as they relate to the extent and implications of their medical recommendations. Scrignar[1] has recently called attention to the medicolegal procedures of the sanity hearing and points out some common pitfalls which may be encountered when physicians participate with members of the legal profession in the determination of an individual's mental competency to stand trial. It requires our understanding of the three stages of the judicial process involved, the pretrial, trial and post-trial phases.

When a lawyer has reason to believe his client may be "insane" and mentally unfit to stand trial he files a motion with the criminal district court judge for a sanity hearing. One or more physicians are appointed to a commission charged with determining the mental competency of the accused to stand trial. This is termed the pretrial stage. It means that the physician is asked to render an opinion about the defendant's ability to understand the nature of the procedure against him, his position in these proceedings and his ability to assist his legal counsel in his defense and only this.

In the legal sense to be mentally competent requires that the defendant's cognitive functions be intact. He must be able to comprehend and understand his position as it relates to his legal status. He must also be able to communicate properly so that he may adequately co-operate with his lawyer in preparation of his case. If these two functions of mind are intact then the defendant is considered mentally competent to stand trial. If either or both are impaired the individual is not mentally competent to stand trial. In this pretrial stage, it is the defendant's competence to stand trial that is the only relevant issue.

Whether or not the defendant is criminally responsible for a crime when it was committed is not the issue in the pretrial stage. The issue is reserved for the trial. It is in the trial stage that the court uses the so-called McNaghten rule as the right or wrong test for the accused actions. The McNaghten rules states that a defendant is not criminally responsible for his acts if he "was laboring under such a defect of reason from disease of the mind, as to know the nature and quality of the act he was doing or if he did know it, that he did not know he was doing what was wrong." Whether or not an individual should be held criminally responsible for his acts because of alleged "insanity" at the time of commission of the act is an issue to be decided during the trial stage. If the accused is now convicted, then ultimate sentencing with the dual goal of protection of society and rehabilitation of the convicted are matters for the post-trial phase.

One of the most common reasons for inequities that may occur, arises from attempts to resolve trial and post-trial issues at the pretrial stage of legal proceedings. Scrigner quotes four types of case histories, illustrating some of the difficulties that may be encountered when physicians and members of the legal profession participate in determination of mental competency to stand trial. One was a case where the physician becomes the judge. It was a case of a paranoid schizophrenic who committed murder. In the state hospital he was adequately treated and appeared able to stand trial. The physician decided he was a potential menace to society and might murder again and was indefinitely committed. He was not permitted to stand trial and his guilt or innocence never to be determined.

Another case cited by Scrignar is where the judge acted as physician. A schizophrenic entered a vacant house, was arrested and put in prison to await trial. After treatment he entered a remission, appeared mentally able to stand trial but didn't because the judge refused to allow him to stand trial and sent him back to the state hospital because "he was taking drugs to be sane." The judge

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...can be rough when epidemics of nausea and vomiting strike a family. Emetrol offers prompt, safe relief. It is free from toxicity[1] or side effects[2,3] and will not mask symptoms of serious organic disorders.

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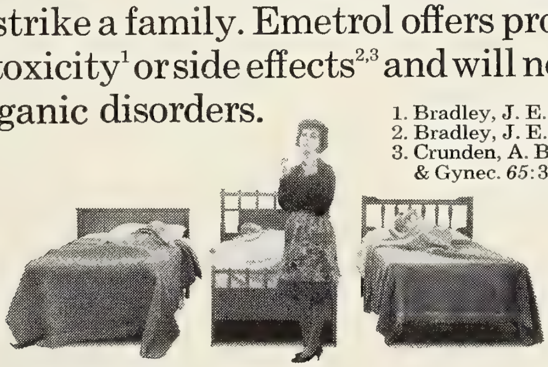

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used his legal rights in matters of medical knowledge. He was not cognizant of medical advances and the soundly established value of antipsychotic agents to maintain mental competence. [2, 3] What he did in effect was to impose a life long sentence and permanent confinement, forever depriving the individual of due process of law.

A third case is where a physician assumes the role of benevolent therapist. A thirty-four year old schizophrenic was arrested for assault and sent to a mental institution. Although the patient became competent to stand trial he had not been allowed to do so because the doctor thought he would benefit from further hospitalization. Had he stood trial and been found innocent he would have had a more successful rehabilitation than being constantly under the threat of having to stand trial.

A fourth case is where the judge acted as protector of society. A forty-eight year old alcoholic was arrested for disturbing the peace. After the alcoholic bout he was oriented, his memory grossly intact, aware of the charge against him but denied personal responsibility. He communicated well with the examining psychiatrist and was considered mentally competent to stand trial. However, the judge knew him personally, decided that the man will get into further trouble with the law and committed him to jail, without allowing him to stand trial. Whether he will get into further trouble was a medical not a legal judgment and at the pretrial stage of legal procedure it was irrelevant. If the defendant understands the proceedings against him and can assist legal counsel in his defense he must receive his day in court. Deprivation of this right could mean life long confinement to a prison-like hospital.

It is understandable that questions run through men's minds at the pretrial stage such as "what if the defendant is found guilty and sent to a state prison?" "What if the defendant is found not guilty because of insanity and sent to a state hospital," or what if the defendant is found not guilty and set free on society? However, they should not influence the question at the pretrial which is merely whether the individual is competent to stand trial. The determination of mental competence to stand trial is an asset of great importance to the defendant. If he is able to stand trial he may be saved permanent incarceration.

Communication between judge and physician regarding the ultimate treatment of the defendant is reserved until later and the conscientious judge is always eager to receive medical counsel which may aid him in the disposition of cases involving mental disorder. Such counsel, however, is appropriate only in the post-trial phase of crime procedure and should be neither sought nor given during mental competency proceedings.

The most common reasons as Scrigner's case histories reveal, as to why inequities do occur is failure to recognize the continuous but separated stages of criminal procedure—pretrial, trial and post-trial and attempts to resolve trial and post-trial issues at the pretrial stage. Without doubt more mutual interaction and cross education between the professions of medicine and law are needed in order to arrive at solutions to exciting problems in these areas and other areas.

L.H.N.

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Extragonadal Estrogen Production

Traditionally we think of gonadal hormone as arising in the gonads. There can however be hormone increments of varying magnitude from extragonadal biosynthesis especially with regard to estrogens and androgens. Under normal circumstances such supplementation is not usually significant, but it can become important in adrenocortical and ovarian disease.

We need to recall, however, that the availability of a particular hormone is not the result only of endocrine secretion, for there is a contribution from the liver for example which is concerned with metabolism of these hormones and with the kidneys that excrete the hormone. Precursors may be converted to active hormones in the liver, and reintroduced into the circulation to augment the total effective concentration of these substances.

The appropriate balance of active hormones can be upset by diminished inactivation or diminished clearance through the kidney resulting in abnormal reintroduction of the hormone into the circulation. As far as testosterone or estradiol is concerned minor quantitative alterations in these processes could lead to abnormal hormonal accumulation of clinical significance. This type of disordered steroid production has in fact been suggested as the basis of female hirsutism. It has also

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anticostive, *adj.* (*anti* opposed to + *costive* causing constipation.) Against constipation. (Now isn't that a good idea in an iron-containing hematinic?)

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Vitamin B_1	7.5 mg
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Vitamin B_6	7.5 mg
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Whether it's a 24-hour "bug", a food problem, or simply nervousness and anxiety, Parepectolin will bring the diarrhea under control until etiology can be determined. In some cases, Parepectolin may be all the therapy necessary.

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Contains opium (¼ grain) 15 mg. per fluid ounce.
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Pectin .... (2½ grains) 162 mg.
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Usual Adult Dose: One or two tablespoonfuls three times daily.

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been implicated in the estrogenicity encountered in liver disease.

Kase and Cohen have reported a case of primary amenorrhea and hypogonadotropic hypogonadism in which a combination of extragonadal sources of estrogen produced severe atypical endometrial hyperplasia, dysfunctional uterine bleeding and endometrial carcinoma. Their patient had absence of pituitary ovarian function. She did however have an extragonadal source of estrogen. It turned out that her adrenals were secreting dehydroepiandrosterone sulphate which was then converted to estradiol probably in the liver. As a consequence an endometrial lesion developed that was potentially of serious clinical consequence.

There is much evidence that the adrenal gland does secrete estrogen. Some of it comes from patients in whom tumors of adrenocortical origin can be markedly feminizing in male patients. Increased estrogen excretion reaching high levels is found in prepubertal children with congenital adrenal hyperplasia. This subsides when they are treated with cortisol. ACTH can markedly increase estrogen excretion in castrates. Furthermore, estrogen persists in the urine of men and women after castration and disappears after adrenalectomy (reviewed by Kase and Cohen).

All these phenomena could be due to secretion by the adrenal cortex of a precursor of estrogen which is then converted to estrogen by the liver. This view is supported by the absence of direct evidence for estrogen secretion by the adrenal and by the fact that the normal adrenal in vitro does not show estrogen synthesis. This would point to the liver as a site of estriol formation and lead us to consider the liver as a key organ in estrogen as well as testosterone synthesis even apart from its well established role in the formation of steroid conjugates.

When it is observed that marked estrogen secretion or even cyclic estrogen secretion occurs after ovariectomy, our first thought hitherto has been that some accessory or super-numerary tissue has been left behind. It is admittedly difficult at times to avoid leaving ovarian remnants behind in operations performed in the presence of adhesions, pelvic inflammation or endometriosis. Kase and Cohen's case did have inactive ovaries low 17-ketosteroids but a significant production of estrogen by the liver from a precursor-dehydroepiandrosterone sulphate. It is a document for the existence of non-gonadel sources of estrogen production which of course is not governed by the usual physiologic controls. As a result the patient suffered from prolonged stimulation of the endometrium without the usual periodic withdrawal or inhibition.

One final problem is the relation between unopposed estrogenic menstrual cycle abnormalities and the high incidence of endometrial cancer. Kase and Cohen's case did show islands of endometrium transformed into cancer. One would have to think that the intensity and duration of an unopposed estrogen stimulus may be a factor operating in the production of endometrial cancer. When there is an estrogen producing source outside the gonads which does not allow for periodic menstrual desquamation in post-menopausal women, there is certainly prolonged stimulation to tissues which might lay the basis for transformation of endometrial tissue to malignant cells.

L.H.N.

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Mount Sinai Medical College Of City University

Jewish immigrants founded Mount Sinai Hospital in 1852. Now its twenty-two building medical complex is located on Fifth Avenue between 98th and 101st. Street. It treats 150,000 patients a year, delivers 5,000 babies and is indisputedly one of the nation's best.[1] It is still not satisfied and it is beginning a medical school. This is a long, costly and intellectually demanding business and the most difficult undertaking any university can attempt. In fact it is nearly a decade since the hospital leaders started thinking about a medical school. Next year they will accept twenty-five year students but will have to wait three years when the school's major building will be completed before accepting the first full-sized class of one hundred. The initial investment to create the school is estimated at $107 million but it will probably exceed this figure.

The hospital has a long tradition of clinical excellence, a high quality staff attracting first class interns and residents and has encouraged research and an atmosphere of inquiry. The school starts with impressive intellectual assets. It also starts at a period of ferment in medical education and can devote its energies to experiment with medical education. This it can do because it is not weighted down by tradition and vested interest and can go ahead with new ideas. The school's first head is George James, former Commissioner of Health of New York City who recognizes the revolutionary changes that are taking place both in medical education, biomedical science and medical practice.[2]

In medical education Sinai is doing three things. It is reducing the standard curriculum now called the "core" and changing the way it is taught. It is leaving far more time for electives and it is introducing a new course "introduction to comprehensive medicine and care of the patient" which should bring students into contact with patients early in the first year. There will be more elective time for students to specialize but the hope is that students will use the elective periods to "experiment." The early bedside experience is intended to broaden the physician by introducing him immediately to patients, thus exposing him also to the economic, ethical and social problems in medicine. In the third and fourth years, basic science concepts will relate to the patient in daily basic science seminars. Most of the required courses (core) will be integrated. Students will concentrate on a particular organ or a particular disease phenomenon and learn what each department has to say, for example about the heart.

There are obvious difficulties. How much "core," how much free curriculum (electives) since every department will want to teach more of its own stuff. The initial plans call for first trimester to be taught along traditional lines as an introduction to the basic sciences before organ and disease oriented study. It will be a sort of dictionary of the basic sciences. Because this requires students to learn too much too quickly, it may require a second trimester.

A second part of the plan is to integrate not only the first two years already accomplished in other schools but also the third and fourth year of clinical studies. This will not mean rotation from medicine to surgery, etc. but rather to study the medical, surgical and even psychiatric problems of a particular organ or illness at the same time. Some areas obviously can be better learned during internship such as obstetrics in the delivery room and dermatology and so Sinai will reduce attention in those areas that can better be learned during internship and residency.

One important area will be upgraded, community medicine. Sinai will treat this field as a major specialty, include in it nutrition, preventive medicine and distribution of medical care. It will develop its own experts and students will be able to devote much of their elective time to studying it. The school's first dean, an expert in community medicine, will also head this department.

The curriculum's fundamental principles are clear. Four years of medical school teaching cannot teach physicians everything and greater emphasis on "principles" will be pursued in the first two years and a de-emphasis on some clinical specialties in the last two years. This stems from the recognition that the most important services a medical school can perform is to impart good habits to its graduates so that they can continue as students for life after graduation. The early introduction to the patient and emphasis on free curriculum will permit the student to spend much of his time working with individual physicians. Medicine is very diversified and growing more so and specialization is virtually inevitable, thus the value of an early chance for the student to explore deeply with electives.

Although the philosophy behind the curriculum is firmly formulated as a workable plan, it has a long way to go and complications are already apparent. Integrated teaching demands a great deal

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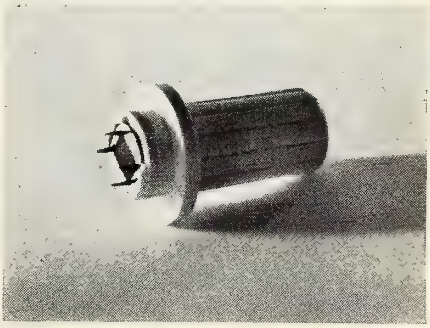

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more of faculty members than did departmental teaching when each teacher was lord of his own class. The new system requires teachers to plan together, to avoid repetition and conciliate honest differences. For integration to work in the clinical years similar preparation will be required. All this consumes time and could conceivably lead to its rejection by some who are more interested in research than in teaching or at least cause resentment.

The real question remains whether all this reshuffling will be worth the effort. Will it bring the patient himself into focus rather than his organs and diseases. There are those who say that the brightest student will prosper regardless of the form of teaching. That it is the teacher's inspiration rather than curriculum that promotes learning. They say that the slow student will encounter difficulty in any scheme and only the "middle third" at best can gain significantly from the reorganization. Since education has become experimental, meaning continuous changes, how long will it take to know whether any scheme is effective and how much effort of the faculty will be required for this continual experimentation?

Besides the curriculum much more is involved in building a medical school. Sinai Hospital, in order to attract researchers, would have had to develop a medical school. Only in this way could it continue to get the best interns who tend to go to hospitals as a part of medical complex in a university setting. But how to find a university to affiliate with. This proved difficult until Albert Bowker former Dean of the Graduate School at Stanford became Chancellor of the City University. With him the affiliation was quickly arranged and federal grants soon followed. With this affiliation recruiting the faculty began to fill gaps in the hospital staff. P. G. Katsoyannis who synthesized human and sheep insulin will head the Department of Biochemistry. Irving Schwartz heads the Department of Physiology. S. W. Berson an authority on peptide hormones and diabetes heads the department of medicine.

Sinai clearly seeks to excel as a medical school. The personality of the school is proud and ambitious. It seeks to do more than alleviate the shortage of physicians. It may collaborate with the City University in a four year Health Center Institute to be established near Sinai. Its purpose is to train skilled medical technicians and teachers for medical technicians at two year colleges and its undergraduates will use Sinai as a learning laboratory. This could conceivably be the start of an expanding program of Community Medicine.

Even though Sinai already has $107 million for the new school it is conceivable that the continuing costs of creating a great medical school are far greater than its founders had anticipated. It will receive $250,000 dollars a year from the City University for support of ten faculty chairs otherwise, the school is autonomous and on its own. But Sinai has a widespread reputation for the generosity and quality of its board of trustees as witness the growth of the hospital over the last century. The medical profession has no doubts about its ability to recruit a faculty of excellence and of raising the necessary funds. Whatever difficulties the future has in store for this great institution, the young recruits for places in the student body have already shown their high regard for it. More than four hundred inquiries have been already received for Sinai's first small class of twenty five. We shall watch this great institution with hope that all its dreams will be fulfilled.

L.H.N.

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CORRECTION

In the article, "CROS Hearing Aids: A Breakthrough for the Unilaterally Deaf Patient and for Others with Special Hearing Problems", by David S. Green, Ph.D., Eiji Yanagisawa, M.D., Howard W. Smith, M.D., D.M.D. which appeared in the December 1967 issue, pages 855-858, the legends for Figures 1, 2, 3, 4, and 5 should be corrected as follows: 1. A schematic of the CROS using an electric coupling (wire) across the head; 2. A schematic of the CROS using an acoustic coupling (hollow plastic tubing) around the head; 3. A schematic of the CROS using an acoustic coupling (hollow plastic tubing) across the head; 4. A schematic of the CROS using an electric coupling (wire) around the head; 5. A schematic of the BICROS in an eyeglass hearing aid.

176TH ANNUAL MEETING

CONNECTICUT STATE MEDICAL SOCIETY

Hartford Hilton Hotel

10 Ford Street, Hartford, Conn.

April 30, May 1, 2, 1968

PRELIMINARY PROGRAM

TUESDAY, APRIL 30

MORNING SESSION

8:00 Registration of Delegates—Mezzanine Floor
Continental Breakfast

9:00 Call to Order—Opening Session—House of Delegates—Terrace Room

12:30-1:30 Luncheon for Delegates and Official Guests—City Rooms

AFTERNOON SESSION

12:30 Registration for Scientific Program—Mezzanine Floor
Opening of Exhibits—Ballroom—Mezzanine Floor

TERRACE ROOM

1:30 Call to Order—President of the Society
Address of Welcome—President, Hartford County Medical Association

1:45 Future and Present Concepts of Population Control
Sheldon Segal Ph.D., *New York City*; Director, Biomedical Division, Population Council, Rockefeller University, New York

2:45 Discussion
John McL. Morris, *New Haven*, Professor of Gynecology, Yale University School of Medicine, New Haven

3:00 Reference Committee Hearings—House of Delegates

3:30 Section Meetings

EVENING SESSION

6:30 Reception and Dinner for Delegates and Official Guests
City Rooms—Mezzanine Floor

8:00 Program by CSMS Committee on Medicine and Religion—Terrace Room

PRELIMINARY PROGRAM

WEDNESDAY, MAY 1

MORNING SESSION

9:00 Registration for Scientific Assembly—Mezzanine Floor

TERRACE ROOM

Symposium on Atherosclerosis

Moderator: Philip K. Bondy, New Haven; Professor Medicine,
Yale University School of Medicine

9:30 A Further Report From the Framingham Study
William B. Kannel, *Framingham, Massachusetts*;
Medical Director, National Institute of Health,
Heart Disease, Epidemiology Study, Framingham

10:15 Biochemical and Clinical Aspects of the Hyperlipidemias Associated With Accelerated Atherogenesis
Robert S. Lees, *New York City*; Assistant Professor and
Associate Physician, Rockefeller University, New York

11:00 Intermission to Visit Technical Exhibits

11:30 New Concepts in the Evaluation of Human Obesity and its Relationship to Disordered Carbohydrate and Lipid Metabolism
Lester Salans, *New York City*; Assistant Professor and
Associate Physician, Rockefeller University, New York

12:15 Panel Discussion
Moderator: Philip K. Bondy
Panelists: William B. Kannel, Robert S. Lees, Lester B. Salans

1:00 Luncheon—City Rooms
Intermission to Visit Technical Exhibits

AFTERNOON SESSION

2:00 Section meetings

3:30 Final Session of House of Delegates—Terrace Room

7:00 Reception—Mezzanine

8:00 Annual Dinner—Dancing—Terrace Room

PRELIMINARY PROGRAM

THURSDAY, MAY 2

MORNING SESSION

9:00 Registration for Scientific Assembly—Mezzanine Floor

TERRACE ROOM

9:30 Symposium on Medical Genetics
Moderator: Herbert A. Lubs, New Haven; Assistant Professor of Medicine and Pediatrics, Yale University School of Medicine, New Haven

Panel: Alfred Knudson, *Stony Brook, New York*: Professor of Medicine, Health Sciences Center, Stony Brook, New York
Leon E. Rosenberg, *New Haven*: Assistant Professor of Medicine and Pediatrics, Yale University School of Medicine

11:00 Intermission to Visit Technical Exhibits

11:30 New Concepts in the Treatment of Medical Shock
Roman DeSanctis, *Boston*; Department of Medicine, Massachusetts General Hospital, Boston

12:15 New Concepts in the Treatment of Surgical Shock
Stanley M. Levenson, *Bronx, New York*; Professor of Surgery, Albert Einstein College of Medicine, Yeshiva University, New York

1:00 Luncheon—City Rooms
Intermission to Visit Technical Exhibits

AFTERNOON SESSION

TERRACE ROOM

2:00 Scientific Program
(Arranged with Connecticut Society of American Board Surgeons)

3:30 Section Meetings

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Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

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THE PRESIDENT'S PAGE

A hue and cry has been raised, and the clamour increases—about RIGHTS. Some claim the right to work; others the right to be paid for not working. The demands also are for the right to food, clothing, a place to live and the best medical care, prophylactic and therapeutic. The right to worship freely is a little less sticky today, but the ethnic groups point up the right to an education and the right to vote and to proper progression in a job.

What is meant by RIGHTS? Some definition and explanation is overdue. The Declaration of Independence includes "life, liberty, and the pursuit of happiness" as "unalienable rights", but then suggests certain requisites to these rights. The signators also proclaimed equality in the creation of man, which must mean that all men are equal in the heart of God and man, for it is all too apparent that they are not equally endowed. Each is an individual and therefore different—and unequal.

Our Bill of Rights guarantees us—in the First Amendment—freedom of worship, of speech, of the press, of assembly, of petition of the government for redress of grievances. And in the Fifth Amendment, we are protected from being held for "infamous crime" without indictment, from double jeopardy for the same offense, from being "deprived of life, liberty or property, without due process of law", and from being compelled to testify against ourselves. Eleven months and a day before the Pearl Harbor debacle, Franklin D. Roosevelt stressed Four Freedoms: freedom of speech and expression, freedom of worship, freedom from want, and freedom from fear.

Are all these rights just for the taking? Who provides them? How do the books balance? RIGHTS must be earned, or must carry with them certain obligations. These basic needs are available at a price. They can be earned in advance, or they can incur a debt. The privilege of RIGHTS carries with it responsibility. If others work to provide food and shelter for anyone, that individual should contribute something to the community: his maximum effort to be contributary, even if only to express appreciation—a spiritual if not a material offering. Some misguided leaders in promoting the rights of certain groups disregard the rights of other groups, even to the extent of promoting lawlessness and violence. Such behavior automatically nullifies those rights. Those who demand jobs and advancement at work must be faithful in attendance and give proper service—or their right vanishes. The right to "life, liberty and the pursuit of happiness" evaporates when it curtails the same right for others. When the press exercises its freedom to the unfair detriment of others, realizing that rebuttals and retractions are neither effective nor given equivalent prominence, it is irresponsible and does not deserve its right.

Respect, responsibility, love, warmth—these are some vital needs today. "Woe unto the world because of offenses, but it must needs be that offenses come, but woe to the man by whom the offense cometh", said Abraham Lincoln, and before closing his second Inaugural added, "With malice toward none, with charity for all, with firmness in the right as God gives us to see the right, let us finish the work we are in, to bind up the nation's wounds, to care for him who shall have borne the battle, . . ."

E. Tremain Bradley, M.D.

ENDURON® | **ENDURONYL®**

METHYCLOTHIAZIDE

Each tablet contains
Methyclothiazide 5 mg. with
Deserpidine 0.25 mg. or 0.5 mg

Indications: Edema and mild to moderate hypertension (Enduron), and mild to moderately severe hypertension (Enduronyl). More potent agents, if added, can be given at reduced dosage.

Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™

Each tablet contains
Pargyline Hydrochloride 25 mg.
with Methyclothiazide 5 mg.

Indications: For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amendable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

TM-TRADEMARK

Contraindications: Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

Warnings: Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery ¼ to ⅕ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

Precautions: Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

Adverse Reactions: Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination.

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Endocrine Effects Of Psychotropic Drugs:

I. GALACTORRHEA AND GYNECOMASTIA

Richard I. Shader, M.D. and Alberto DiMascio, Ph.D.

This is the first in a series of articles which will survey the effects of psychotropic drugs on endocrine function. Much inconsistency exists in the literature about the endocrine effects of psychotropic drugs which may, in part, be explained, 1) by variations in dosage levels, duration or route of administration; 2) by differences in methods of endocrine function assessment and sources for error within these methods (e.g., the bioassay methods for gonadotropins); and 3) by observable host factors such as the degree of anxiety, tension, depression or turmoil at the time of study. Since it is quite likely that each individual has a unique "endocrine signature" or pattern of endocrine response, it is also necessary to consider such factors as the functional status and the basal or initial values (Wilder, 1957) for each gland or level within the complex hypothalamic-pituitary-end organ feedback circuits.

Nonpuerperal galactorrhea and gynecomastia are now well established as sequelae following the administration of a variety of psychotropic drugs. Normal human breast development in its earliest stages proceeds under the influence of estrogen, glucocorticoids and growth hormone (somatotropic hormone). Subsequent development is also influenced by progesterone and prolactin (lactogenic hormone). The actual secretory phase is primarily under the control of glucocorticoids and prolactin. The exact mechanisms of lactation continue to be debated, however, as it has also been theorized that high levels of estrogen are by themselves inhibitory, while low levels are lactogenic (Relkin, 1965). The role of the median eminence of the hypothalamus in the regulation of lactation is of paramount importance since the secretion of prolactin from the anterior pituitary is under the tonic inhibitory control of prolactin inhibitory factor (Reichlin, 1966).

Gynecomastia in males may occur from increased secretion of luteotropic hormone through its direct effects on mammary tissue or from the effects of increased gonadotropic hormones on the production of estrogen by the testes. When estrogen secretion is high, gynecomastia may develop in susceptible mammary tissue.

The frequency of the reported occurrence of galactorrhea is quite variable (0% to 80%). Clearly, this variation, in part, is related to the potency of the drug itself in producing this effect, to the dose and duration of drug administration, and to host factors both in the target organ itself and in the hypothalamic-pituitary-mammary gland axis. One additional factor must be considered, namely, how the galactorrhea is elicited. For example, squeezing the nipple may reveal the presence of galactorrhea in some subjects in whom it might otherwise go unrecognized if the criteron for its presence is the patient's self-report of frank discharge. Ayd (1955) reports that lactate could be expressed from the breasts of "approximately 80%" of women receiving chlorpromazine.

Galactorrhea was reported in women taking chlorpromazine by Cohen (1955) and Kinross-Wright (1955). Numerous reports have appeared since that time indicating that galactorrhea can occur at varying dose levels, may appear as early as eight days after the onset of treatment, and is found more commonly in premenopausal women (de Weid, 1967). Galactorrhea has also been noted in patients receiving thioridazine, trifluoperazine, prochlorperazine, and fluphenazine (Hooper, et al, 1961). Galactorrhea has been reported with imipramine (Klein, M., 1964; Klein, J., et al, 1964), meprobamate (Hooper, et al, 1961), chlorprothixene (Vinãrova and Tachezy, 1965), thiothixene (Simeon, et al, 1967), and haloperidol (McNeil, 1967). It is probable that galactorrhea

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occurs with all psychotropic drugs that suppress the secretion of prolactin inhibitory factor in the hypothalamus (median eminence). Further evidence for this hypothesis comes from the work of Mishkinsky (1966), who demonstrated that a crystal of perphenazine stereotaxically placed on the median eminence in female rabbits results in marked mammary development and copious lactation. It has also been pointed out that a dissociation exists between the mammotropic activity and psychotropic properties of a drug. Khazan and coworkers (1966) have demonstrated that perphenazine sulfoxide and chlorpromazine sulfoxide, which lack tranquilizing action, are capable of lactogenic action in estrogen-primed rats, and that a change from Cl in chlorpromazine to Br, bromopromazine, produces an increase in mammotropic effects without change in sedative effects.

The galactorrhea which occurs in females is frequently accompanied by some degree of breast enlargement or engorgement. Breast enlargement in males has rarely been reported. One case has been reported (Arroyo, 1966) with the monoamine oxidase inhibitor, phenelzine, and it has also been reported in tuberculosis patients receiving isoniazid (Koang, 1957; Molina, et al, 1957). Three cases have recently been reported (Margolis and Gross, 1967) with phenothiazines, one each with thioridiazine, trifluoperazine, and chlorpromazine. It is of interest that the thioridazine effect was reversed when chlordiazepoxide was substituted, even at a chlordiazepoxide dose of 750 mg daily. Two additional cases associated with hyperpigmentation of the areola and mild secretion have been reported following high doses of trifluoperazine (Cortez and Durazo, 1963). Gynecomastia has also been reported in one adolescent male receiving haloperidol (McNeil, 1967).

The following case reports illustrate nonpuerperal galactorrhea and gynecomastia.

Case 1). A single nulliparous woman, aged thirty-two years, with chronic schizophrenic symptomatology was seen in consultation after she had been receiving chlorpromazine (average daily dose 400 mg) for six months. Four days before, she had noticed a watery, white fluid which spontaneously appeared at the nipple of the right breast. A similar fluid could be expressed from the left breast. Both breasts were slightly enlarged and diffusely tender to palpatation. On questioning, she stated that her brassiere had not been fitting comfortably for about one month. She had missed one menstrual period. Chlorpromazine was lowered to 150 mg/day. Three weeks later her menstrual flow had returned, her breasts were no longer enlarged and tender, and fluid could no longer be expressed from the nipple. Her psychotic symptomatology could also be controlled at the lower dose.

**Case 2).* A single Negro male, aged twenty-two years, with symptoms of an acute undifferentiated schizophrenic reaction showed evidence of jaundice and hepatocellular damage after receiving chlorpromazine (average daily dose 300 mg) for three weeks. Two months later he was placed on thioridazine. His average dose over the following month was 450 mg/day. Six weeks later, when his daily dose of thioridazine was 200 mg, he complained of increasing breast tenderness bilaterally. Even gentle palpation was painful. The left breast appeared slightly enlarged with minimal proliferation of glandular elements. No fluid could be expressed from either side. Thiordiazine was discontinued and trifluoperazine was begun. His breast symptoms gradually subsided over the next month. This patient also developed the typical ejaculation disorder seen with thioridazine (Shader, 1964), which began within a few days of starting thioridazine and subsided within several days following the discontinuance of that drug. Although the contribution of the liver pathology to the development of his gynecomastia cannot be determined with certainty, it seems entirely possible that altered estrogen detoxification secondary to the hepatocellular damage may have been involved in the subsequent development of the breast pathology.

Galactorrhea is a common side-effect of a number of psychotropic drugs. It most commonly occurs with long duration, high dose, phenothiazine regimens and is often accompanied by amenorrhea. Dose reduction is usually sufficient, although it is occassionally advisable to switch to another drug. Gynecomastia in males is infrequent, and should be similarly treated.

**We wish to thank Mark L. Stiglitz, M.D. for calling our attention to this case.*

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State Health Department Announces Cervical Cancer Study

Since 1950, mortality rates for cervical cancer have been declining. Although most of this decline is frequently ascribed to the effectiveness of Papanicolou screening programs, it should be noted that the decline began just before screening was introduced. and even now only approximately 25% of women over age 20 are screened in any one year. Moreover the decline in mortality has occurred among post-menopausal women who are the least likely to have had the Pap test. Thus the question is often asked if the Pap test alone is responsible or what other factors in addition may have influenced the changes in rates.

A research study to be undertaken by the Chronic Disease Control Section of the Connecticut State Department of Health and the National Cancer Institute will investigate some of these factors, such as the rise in the number of *total* hysterectomies performed, and increased availability of medical care (especially postpartum care) which helps to detect and treat potentially dangerous cervical conditions. The influence of the Pap test programs will not be neglected in the study, but an attempt will be made to assess its impact, especially on the two groups thought to be most vulnerable to cervical cancer—post-menopausal women and those in lower socio-economic groups.

One part of the investigation will consist of a short questionnaire mailed to the attending physicians of all cervical cancer patients diagnosed from 1959 to 1964. Primarily, it will cover the use of the Pap test and other diagnostic techniques, the presence of pathological cervical conditions, and pregnancy history.

From the replies, it may be possible to assess the frequency with which the Pap test should be done, and to evaluate areas where Pap tests need increased acceptance. It is also hoped to be able to pinpoint which factors can be stressed in the future to bring about continued reduction in mortality at all age levels.

A Guide To Synovial Fluid Analysis

Siegfried J. Kra, M.D.

The diagnosis of the type of arthritis involving one or many joints may be ascertained through the aid of only a few laboratory examinations. Tests for rheumatoid factor in the serum may confirm the diagnosis of rheumatoid arthritis. Negative finding of this test does not always disprove the presence of this disease. Similarly, the LE phenomenon often is negative in the early stages of systemic lupus erythematosus. The serum uric acid level is affected by such medications as diuretics or large doses of aspirin that the patient may be taking concurrently. Likewise, X-ray changes of patients with rheumatic conditions may not occur until late in the course of the disease. Examination of synovial fluid from a swollen joint, however, may give specific results. This test is inexpensive, can be performed in a physician's office, and requires little equipment. The purpose of this report is to describe a brief and simple diagnostic aid in the examination of synovial fluid.

Technique of Aspirating Fluid from a Joint

Fluid is easily obtained from a swollen, injured knee without causing the patient too much discomfort. As in all surgical procedures, a perfectly aseptic environment must be provided. The skin overlying the joint is thoroughly cleansed with an antiseptic agent and then painted with another antiseptic agent and allowed to dry. The point of entry of the needle is commonly on the medial aspect of the knee, but I have found that direct entry at the lateral aspect of the knee, where the synovium is the fullest and the skin most taut, is the most convenient and painless procedure. The patient should be lying comfortably in a fully extended position, a rolled towel under the popliteal space. On hand should be a tube containing anticoagulant, a tube for culture, and a plain tube. A 20-gauge needle with a five or ten cc. syringe is inserted, and with gentle aspiration, soon reaches the suprapatellar pouch, at which point fluid usually gushes into the syringe. The feeling of a slight resistance before the synovium is penetrated is similar to the resistance felt during thoracentesis when the pleura is reached. At this point, the patient may experience slight discomfort. After aspiration has been completed, ice may be applied to the joint for ten to fifteen minutes. Post-synovial aspiration infections are a very rare occurrence and need not be feared if the procedure is followed accordingly.

Examination of the Synovial Fluid

Simple gross examination of the fluid determines its color. The presence of blood in large amounts usually signifies a hemarthrosis. Normal fluid is straw colored and odorless. Grayish fluid is usually purulent. If an acute synovitis is present, the fluid may be cloudy and darkish yellow, as in rheumatoid arthritis; or it may be milky white as in chronic gout. The viscosity of the fluid is easily ascertained by simply placing a drop on the index finger. Normal fluid will become stringy when rubbed with the thumb. Absence of stringiness is indicative of acute synovitis from rheumatoid disease, gout, or septic arthritis.

Mucin Clot Test

Normal fluid contains a protein polysaccharide complex called mucin which forms a clot.[1] The test for the mucin clot is performed by adding two or three drops of synovial fluid to 5% acetic acid in a test tube. If the mucin is of normal consistency, a firm clot will form. In active synovitis, no clot will form and there will be fragmentation. A poor mucin clot is found in rheumatoid arthritis, Reiter's syndrome, and infectious arthritis. A white blood count should then be done under high power, using saline as the diluent instead of ordinary white cell counting solution, with a smear of synovial fluid stained by Wright's stain technique. A marked increase in the white cell count from 35 to 50,000 might be found in rheumatoid arthritis or infection arthritis in contrast to osteoarthritis in which there is a white count of 2,000 to 3,000. A differential count may reveal a predominance of polynuclear cells in rheumatoid fluid as well as in gout and infectious fluid. The portion of the synovial

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fluid without anticoagulation may be used to determine the presence of the rheumatoid factor.

Examination of Synovial Fluid for the Rheumatoid Factor[2]

This is a very simple procedure requiring little equipment. I use the Hyland Slide technique.* Agglutination of the synovial fluid is seen when one drop of the patient's synovial fluid is mixed with one drop of the Hyland test solution. A positive test indicates the presence of rheumatoid factor in the synovial fluid even though the serum may be negative for the rheumatoid factor.

Microscopic Examination of the Fluid

A drop of the fluid is placed on the microscopic slide with a cover slip under 450X magnification. The fluid is examined for uric acid crystals and the nature of the white blood cells.[3] Uric acid crystals are needle-like structures consisting of monosodium urates and found either floating freely in the fluid or phagocytized by the white blood cells. (See figure.) If phagocytized, the uric acid crystals will be seen crossing a white blood cell. These crystals are pathognomonic of gouty arthritis. They are particularly helpful when serum uric acid level is normal in patients with gout or when uric acid is elevated from medications such as thiazides or small doses of aspirin. Other odd-shaped, shorter, and more rectangular crystals also may be seen floating freely or phagocytized by polynuclear cells within the white blood cells. These are calcium pyrophosphate crystals which may be responsible for recurrent swelling and pain in the joint and mimic gout, called by some authors pseudo gout, or chondrocalcinosis. [4,5] These crystals do not polarize under polarized light and are weakly birefrigent when viewed under the microscope. The picture is seen better under polarized light which, however, is not necessary for identifying these crystals as they can be seen under oil immersion with a closed light condenser. Any microscope can be easily adapted for a polarized viewing by inserting a polarized disk into the condenser in the eyepiece. The eyepiece is then rotated until the darkest position is reached.

Careful study of the white blood cells may reveal definite cytoplasmic inclusions found in rheumatoid arthritis, gouty arthritis, and septic arthritis.[6] They appear as black granules which normally do not appear in white blood cells and are considered to represent phagocytosis of rheumatoid factor. This thread-like particles representing autolysis of surrounding cartilage or phagocytic lysosomes must be differentiated from the crystals of gout and pseudo gout. A culture and sugar determination of the synovial fluid should be done routinely on every aspiration as they are helpful in diagnosing infectious arthritidies such as gonococcal arthritis. In the latter, the synovial sugar is markedly reduced.[7] A hemosiderin stain can sometimes be made on the fluid for the determination of its iron content as arthropathy has been reported in hemachromatosis.[8] The synovial fluid may be grossly hemorrhagic, resulting from a traumatic puncture, villonodular synovitis, hemophilia, or trauma.

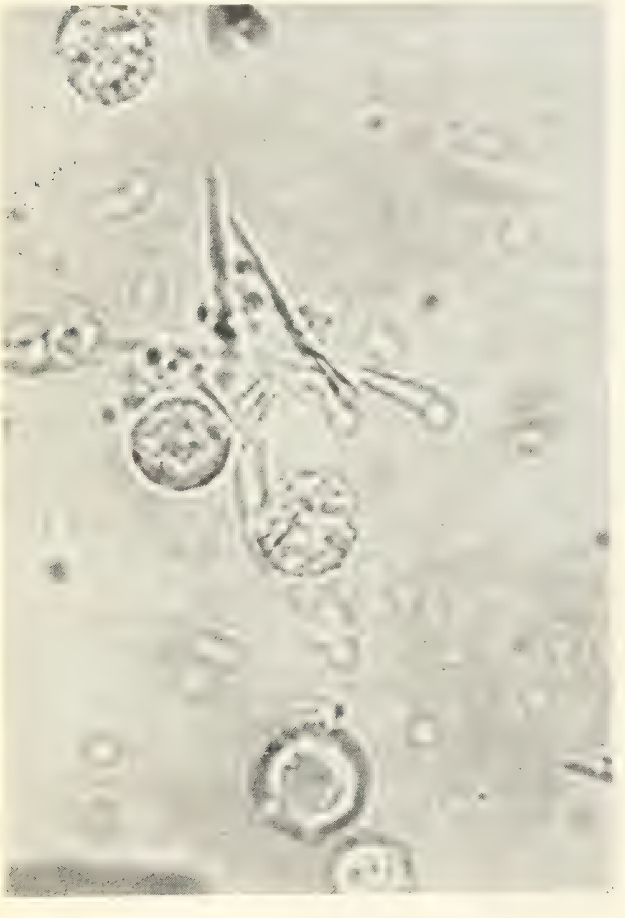

FIGURE 1. Urate crystals in synovial fluid, polymorphonuclear leukocytes containing typical cytoplasmic inclusions in wet preparation of synovial fluid of rheumatoid arthritis. (Microphotographs by Siegfried J. Kra, M.D.)

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*Hyland RA-Test
Hyland Laboratories
Los Angeles, California

Interpretations in Various Types of Arthritides

Osteoarthritis may present in a middle-aged person with a joint effusion. The mucin clot is good. The white count is rarely over 11,000 and will consist of primarily lymphocytes. The viscosity will be normal and generally there will be absence of crystals unless advanced osteoarthritis occurs, at which time calcium pyrophosphate crystals may be seen. In *rheumatoid arthritis* characteristic types of granules may be seen in the white blood cells, which are believed to be rheumatoid factor complexes, or, so-called "RA cells." It is felt these rheumatoid factor complexes, or, "RA cells" represent rheumatoid factor phagocytized by white blood cells. The viscosity will be poor with a poor mucin clot. The white blood count may rarely be normal or as high as 50,000 with a predominance of polynuclear cells. No cartilage debris will be seen and the fluid may be clear to cloudy. *Gouty arthritis* may present with a clear fluid or cloudy fluid with a poor mucin clot and a low viscosity and a white count generally over 12,000 with a predominance of polynuclear cells. Granular inclusions may be present in the white blood cells. This fluid can readily be differentiated from rheumatoid arthritic fluid by the presence of urate crystals. In a *septic joint,* the fluid is purulent with a poor mucin clot, a low viscosity, and a white blood count of over 70,000 with at least 90% polynuclear cells. Inclusions may also be seen in the white blood count. A sugar determination on the synovial fluid will demonstrate a very low level. *Rheumatic fever,* with transitory synovitis, is very difficult to differentiate from rheumatoid arthritis. The synovial fluid in patients with rheumatic fever will have normal mucin clots with low viscosity and white blood counts in the range of 10,000 with at least 50% polynuclear cells. *Disseminated lupus erthematosus* can initially present clinically with the picture of rheumatoid arthritis. The lupus phenomenon may be absent in the blood. However, a Wright stain of the cells from the synovial fluid may demonstrate numerous LE cells.[10] The fluid should first be centrifuged and the sediment stained. Demonstration of the LE cells does not require incubation techniques as in the examination for the lupus phenomenon in the blood. The fluid of lupus is generally yellow. The mucin clot is good and viscosity normal. Lupus erythematosus is the only condition other than osteoarthritis in which the white blood count is generally lower than 3,000 with a few polynuclear cells and lupus cells present on the smear. The major difficulties encountered in synovial fluid interpretations is distinguishing classical rheumatoid arthritis from rheumatoid variants, such as psoriatic arthritis, ankylosing spondolitis, and the arthritidies associated with agammaglobulinemia and ulcerative colitis. However, the clinical findings of psoriatic arthritis, ankylosing spondolitis, and the arthritis of ulcerative colitis may be clearly characteristic and will help to differentiate between these diseases as when the synovial fluid is of little help.

Clinical Studies

During a two and a half year period, 250 arthrocenteses have been performed in my office with the diagnostic procedures outlined above. Not one infection or hemorrhage has resulted from this procedure. Fifty of these cases were diagnosed clinically to have a specific rheumatic disease. In 200 cases, the synovial fluid analysis was extremely helpful in the diagnosis. In fifty of these cases, only the synovial fluid analysis made the diagnosis of the type of arthritis possible. Fifteen cases had typical urate crystals in the fluid, in spite of the fact that the serum uric acid was normal. Three cases presented with calcium pyrophosphate in the synovial fluid. One patient had numerous LE cells in the synovial fluid and typical findings of rheumatoid arthritis—positive rheumatoid factor present in the fluid, white blood cell counts of about 50,000 and serum rheumatoid factor very weakly positive to negative. In seven cases, fluid was found to be compatible with degenerative arthritis.

Conclusion

The examination of the synovial fluid is a simple and inexpensive office procedure which can be performed routinely when an effusion of unknown or unconfirmed etiology is present in the joint.

Diseases That Can be Diagnosed by Synovial Fluid Analysis

1. Gout
2. Pseudo gout
3. Rheumatoid arthritis
4. Systemic lupus erythematosus
5. Septic arthritis
6. Osteoarthritis

DISEASE	WHITE CELL COUNT	MUCIN CLOT	APPEARANCE	FEATURES
Normal	900-500	good	Clear, yellow	
Rheumatoid Arthritis	12,000-40,000 PMN	poor	Cloudy & Clear	"RA-cells" Latex positive in fluid
Systemic Lupus Erythematosus	3,000	poor		LE-cells on smear of fluid
Osteoarthritis	1,000	good	Clear, yellow	
Gout	12,000± 75% PMN	poor	Cloudy, yellow	Crystals Urate
Pseudo Gout	8,000+ Pred. PMN	poor	Yellow	Calcium crystals
Septic Arthritis	80,000 90% PMN	poor	Purulent Bloody	Glucose decreased

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The Connecticut State Medical Society
176th ANNUAL MEETING
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A Comparative Clinical Study Of A Prepared Childbirth Program

Clarence D. Davis, M.D. and Joseph F. J. Curi, M.D.

In the United States today, over ninety-five per cent of deliveries take place in hospitals under medical supervision. Undoubtedly the three major reasons for this are: (a) the nearly universal prevalence of prenatal care among private patients; (b) the increasing number of people with hospital insurance, and (c) improved obstetrical management, particularly of toxemia, hemorrhage and infection. Today only one tenth as many mothers die in childbirth as did forty years ago, and the current figure still can be reduced significantly.

Because of the shift of labor and delivery from the home and all its attendant familiarity to the hospital, with its associated strangeness, formality and fear-provoking potentialities, much ancillary interest in the relief of childbirth pain has developed. There are several technics to choose from for the safe and relatively comfortable conduct of parturition. These vary from different pharmacological approaches to numerous psychophysical training methods.

When considering these methods as practiced in Europe and the United States, the divergent philosophies and approaches can be separated, as suggested by Buxton,[1] into four categories: *autogene training, hypnosis, psychoprophylaxis,* and *natural* or *prepared childbirth*—depending on the aspects of training deemed most important, as well as the geographical location and sometimes even political persuasion.

Autogene Training A combined psychological and physical approach, using self-hypnotic suggestive technics through a process of training exercises, is called Autogene Training, or as characterized by Buxton,[1] "The Power of Negative Thinking."

Jacobson,[2] in 1929, proposed practice in passive relaxation in the treatment of many somatic as well as psychosomatic illnesses. Schultz[3] has applied this philosophy to obstetrics, contending that adequate relaxation is necessary to relieve childbirth pain. This method stresses self-hypnosis.

Hypnosis. The actual use of hypnosis to control the discomforts of childbirth emphasizes dominance by a qualified hypnotist. The mesmeric method of analgesia and anesthesia in obstetrics has been in practice since Esdaile's experiments in the 1840's, and the hypnotic potency of these technics is reflected by its recently reported use in cesarean section. [4,5] Admittedly, practitioners of the other psychophysical methods can have a "hypnotic effect" on the conscious parturient patient, simply on the basis of persuasive suggestibility. This, however, is not "true hypnosis" or artificially induced sleep. Although frequently successful as a method of pain relief in childbirth, and advantageous in the elimination of pharmacological dependency, hypnosis "does not permit a woman to participate in the process of labor and delivery nor provide her with the satisfaction, sense of accomplishment, and 'joy of childbirth' which are provided by other methods which are said to make valuable contributions to the mother's psychological health and equanimity." [1]

Psychoprophylaxis. This was introduced by Nicolaiev,[6] Volvowski, and the Neo-Pavlovian school in Russia in 1945, and by Lamaze in France in 1952, and is based on Pavlov's concept of conditioned-reflex training. Basically, these technics for painless childbirth maintain that training enables a parturient to eliminate painful sensations by providing a counter stimulus. The objective is the total suppression of the painful characteristics of the sensations during the course of childbirth. Proponents of this method stress that it differs from the passivity of hypnosis in that it is based

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on the active remolding of the patient's consciousness so as to make her realize that pain is not a necessary attribute of labor. It has been admitted that this technic is only a further development in new social conditions of Read's natural childbirth method.[7]

Prepared Childbirth. Natural childbirth, as described by Read[7] in 1933, was based on the supposition that pain in childbirth was a non-physiological response produced by fear, apprehension, and tension. By elimination of these psychological attitudes toward labor and delivery, which he thought stemmed from the traditions of western civilization, Read maintained that pain would be relieved and parturition would proceed in a painless, psychological, "natural" manner. He contended that the fearful and apprehensive mental attitude of the modern woman toward labor produced tension which in turn resulted in the inability to relax. In combination, these factors led to pain, and thus the cycle, 'fear-tension-pain syndrome' was established. With proper education and psychological thinking he proposed to break the cycle by eliminating fear and teaching the patient to relax. Assisted by the psychotherapeutic technic developed by Heardman,[8] who believed that women should train themselves for the physical exertion of labor, Read initiated a combined technic of psychotherapeutic training and physical exercise which became known as "natural childbirth." As Buxton summarizes, "His (Read's) magnetic and persuasive personality, the reaction of both laymen and the medical profession toward extensive use of analgesia and anesthesia and the desire of many women to have their baby in a 'natural' way has possibly resulted in the very popular movement which gained many adherents among patients and physicians alike." [1]

Shortly after the end of World War II, Dr. Herbert Thoms, then Professor of Obstetrics and Gynecology at Yale, popularized this method in the United States. Thoms,[9] however, did not approve of the term "natural childbirth", for he considered it an unfortunate term in many ways, as it suggested to many a synonymity with the primitive, and at the same time, easy childbirth. Antropological reports state again and again that primitive women are not free from abnormal labors and/or excessive pain. Neither Thoms nor Read advocated the disuse of pharmacological obstetrical aids. However, both felt that the great contraindication to the administration of any analgesia or anesthesia was the absence of pain.

Thoms[9] emphasized and re-emphasized the fact that a "prepared" woman who finds herself in need of artificial help and complete anesthesia should not think of herself as a failure and wanting in strength of character. The false assumption of the above has done much to lead to unjustified criticism. The woman is told about the use of analgesic and anesthetic aids and that these are not withheld should they become necessary to the proper conduct of labor and delivery.

Support during labor provides an atmosphere of friendliness, interest, understanding and encouragement, coupled with effective comfort-producing measures which enable the mother to put forth her best effort. Thoms placed great emphasis on "support during labor" and maintained that its effectiveness depended on the sympathy and interest of those in attendance as well as their comprehensive understanding of the patient training, and physical and psychological aspects of childbirth.

There have been many studies extolling the virtues of the Prepared Childbirth Program. However, some have reported insignificant differences. Recent investigations have been carried out at Yale by Davis and Morrone,[10] who state: "The crux of the problem is that we all know what we want to evaluate but do not know how to design the ideal experiment that will eliminate bias, have properly selected controls, and not introduce too many imponderables." This study included 463 patients, 355 of whom were prepared, and 405 of whom received support. The first stage of labor was significantly longer for the support group than for the non-support group. There was no difference between the prepared and unprepared groups. Moreover, the duration of the second stage of labor was not altered by preparation or support. The use of anesthesia was essentially the same for all groups. It was concluded that "the type of person who elects preparation is more important in determining its effect than the preparation itself."

The following pertinent question was raised: "It is not entirely clear why our data do not substantiate previous reports concerning effects of preparation on support, on length of labor, reduction of sedation, etc. Could it be that with the passage of time the original evangelical zeal is gone, and that the major contribution of the prepared childbirth program in this country will ultimately prove to be its help in reversing the trend toward 'heavy' sedation and the use of amnesia-producing drugs?" [10]

Many of New Haven's private obstetricians have directly or indirectly worked with Drs. Thoms, Buxton and Davis in the Yale Prepared Childbirth Program, and thus are well versed in the philosophy, technics and goals of the method. For the most part, these physicians are proponents of the "light analgesic and anesthetic" management of parturients, and therefore differ from their "heavy sedation" colleagues in much of the rest of New England. Since their psychological and medical approaches to obstetrical patients are well versed and directed by the tenets of the prepared childbirth philosophy, numerous questions can be formulated. Do the objective and subjective observations of a group of *program trained* women differ from an *unprepared control* group who are managed by the same private physicians? Are the present results different from those observed at Yale ten years ago? Are the private obstetricians aware of the differences in the management of the trained and untrained groups? Finally, are the trained program women and unprepared controls satisfied with their respective experiences?

Methods and Materials

A group of 141 private primiparous patients was studied. They were followed in labor and delivered in the Memorial Unit of the Yale-New Haven Hospital between June 1, 1963 and September 1, 1963.

The *Unprepared Control Group* consisted of 86 patients who had not participated in any formal preparation program. The *Program Trained Group* comprised 55 women, all of whom were enrolled in the Yale Prepared Childbirth Program.

The prepared group had the following predelivery program outline, with the purpose of providing an opportunity for the expectant parents to develop knowledge and understanding of their childbearing experience.

Mothers Classes and Exercise Program were divided into several sessions during which the following topics were covered by an obstetrical nurse and obstetricians:

1. A. *Introduction to course*

   B. *Exercises*
      1. Posture
      2. Tailor position
      3. Abdominal breathing
2. A. *Anatomy and Physiology* (Obstetrician)
      1. Anatomy
      2. Conception, implantation, placentation
      3. Growth and development of the fetus

   B. *Exercises*
      1. Relaxation on side and abdominal breathing
      2. Progressive relaxation
      3. Review
3. A. *Pregnancy*
      1. Body changes
      2. Uterus
      3. Breasts
      4. Body fluids
      5. Diet
      6. Rest and activities
      7. Clothes
      8. Explanation of breast care demonstration

   B. *Exercises*
      1. Review
      2. Squatting
      3. Pelvic rocking (for backache)
      4. Costal breathing
4. A. *Labor and Delivery*
      1. Onset
      2. Contractions
      3. Effacement and dilatation
      4. Stages
      5. Analgesia and anesthesia
      6. Episiotomy

   B. *Exercises*
      1. Review
      2. Tightening
      3. Pushing
      4. Panting
5. A. *Review delivery — Baby Care — Postpartum*
      1. Admission to hospital and routine
      2. Preparation for baby
      3. postpartum period — activities, attitudes, exercises

   B. *Exercises*
      1. Review
      2. Rehearsal for labor and delivery
6. *Tour*
7. *Breast Care demonstration* (optional)
   For those who plan to breast feed with permission of their obstetrician.
8. *Baby Care demonstration* (optional

The educational lectures have two basic objectives:[1]

1.) An attempt to disabuse the patient of traditional unfortunate folklore associated with the process of parturition.
2.) A clarification of the mechanics and mechanisms of childbirth so that the patient will more readily understand that the process of labor and delivery can be normal and entirely undamaging.

Parents Classes were attended by the huge majority of the couples of the *program trained* women. Four evening sessions—Pregnancy, Labor and Delivery, Parenthood and Infancy—were offered and there was concentration on mutual parental responsibility. During both types of classes, informal discussion and group participation are encouraged. Moreover, every effort is made to clarify thought-provoking terms (laceration, rupture, hemorrhage, etc.) that are integral parts of common obstetric verbiage. Along these same lines, word substitutes are employed, i.e., contractions for labor pains. Without doubt, some of the *unprepared control* patients also attended Parents Classes.

A supplementary reading list is supplied.*

Each *program trained* patient received support during labor by her doctor, assigned nurses or the senior author, in a single, quiet, comfortable and pleasant room. Soft, relaxing music was optional. Each observer helped to maintain a cheerful attitude by providing an atmosphere of friendliness, interest, understanding and encouragement. The parturients were told in advance what to expect, what examinations were to be performed, and why they were necessary. Husbands were encouraged to assist their wives during labor by reassurance and relieving discomfort by back massage, etc. In essence, the program trained mother was made the central figure. The unprepared control group did not receive special support during labor by the nursing staff or the observer, and frequently not by her obstetrician.

From each study group, 50 patients were selected on the basis of their age, private obstetrician, and relative socio-economic standing based on the occupation of the husband, to comprise the comparative clinical investigation. Those having cesarean section were excluded. The age groupings are presented in Table I. In total, 18 private obstetricians supplied the 100 patients. The relative socio-economic levels of the mothers are summarized in Table II.

TABLE I

AGE DISTRIBUTION

	Program		*Control*	
	No.	*%*	*No.*	*%*
Under 21 years	3	6	8	16
21 - 25	23	46	25	50
26 - 30	20	40	14	28
31 - 35	4	8	3	6
TOTAL	50	100	50	100

Mean Age: Program 24.5 years (S.D. 3.2)
Control 23.8 years (S.D. 3.8)

TABLE II

SOCIO-ECONOMIC STANDING

	Program		*Control*	
	No.	*%*	*No.*	*%*
HUSBAND'S OCCUPATION				
Educators, Clergy, Social Workers	5	10	6	12
Clerks, Factory Workers	9	18	11	22
Business World Affiliates	8	16	12	24
Professional Men	10	20	8	16
Students	18	36	13	26
TOTAL	50	100	50	100

Apgar ratings were made in conjunction with the attending medical staff. As soon as convenient, the attending obstetrician was asked to discuss the following questions:

1. Was pain controlled throughout labor?
   Good___ Fair___ Poor___
2. Was the mother cooperative throughout labor?
   Good___ Fair___ Poor___
3. Was she pleased with the results of the technics use? Good___ Fair___ Poor___

One day postpartum, each *program trained* participant was given the following questionnaire:

1. Are you satisfied with your experience?
   Yes___ No___ Indifferent___
   Comments:
2. Would you select Prepared Childbirth next time? Yes___ No___ Indifferent___
   Comments:
3. Which part of the program was most important? (Please number 1, 2, 3, etc., in order of preference, if item is associated with your experience.)
   a) Mothers Classes

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*Thoms — *Childbirth with Understanding*
Thoms — *Our Obstetric Heritage*
Goodrich — *Natural Childbirth*
Wiedenbach — *Family-Centered Maternity Nursing*
Eastman — *Expectant Motherhood*
Buxton — *A Study of Psychophysical Methods for the Relief of Childbirth Pain*
Spock — *Pocket-Book of Baby and Child Care*
Maternity Center Association — *Pamphlets*

b) Exercises
c) Support during labor
d) Husband's presence during labor
e) Doctor's office consultation
f) Other
Comments:

Results and Discussion

The results of the three-month comparative clinical study of the Yale Prepared Childbirth Program are presented in Tables III to X, and are discussed in the following section.

Table III summarizes the dosages of the analgesic medication administered intramuscularly. The equivalent units were estimated as follows:

1 Unit equals 50-75 mg. of Meperidine*
or 30 mg. of Alphaprodine HC 1**
2 Units equal 100-150 mg. Meperidine
or 60 mg. of Alphaprodine HC 1
3 Units equal 175-225 mg. Meperidine
4 Units equal 250 mg. or more of Meperidine

Although the mean dosage was less for the program group, the difference was not statistically significant. It is interesting to note, however, that 20% of the prepared patients required no analgesia, compared with 4% for the control group. In 1954 at Yale, Thoms[11] reported that 34.2% of his program patients required no analgesia, and 62.0% of the remaining participants had a single dose of less than 125 mg. of Meperidine. In Read's study,[12] 50% of the subjects had no analgesia or anesthesia. Other investigators report similar results. [13, 14] Some control studies reported no differences.[15, 16, 17]

Table IV presents the types of anesthesia used. For clarity, the procedures are divided into local, conduction and inhalation. Local anesthesia was employed as the sole means in 52% of the program patients, and 30% of the control patients. Whereas, inhalation anesthesia was resorted to in only 12% of the program women, it was utilized in 28% of the control women. When applied to statistical analysis, these differences were significant. Thoms[11], on the other hand, found that 95.2% required local anesthesia only. Other investigators had similar conclusions. [13,18] Davis, et al.[10] and others[17] report no significant differences.

Table III
Preanesthetic Medication

Total Dosage	*Program* *No.*	*%*	*Control* *No.*	*%*
1 Unit	21	42	26	52
2 Units	14	28	17	34
3 Units	5	10	4	8
4 Units	0	0	1	2
No Preanesthetic Medication	10	20	2	4
TOTAL	50	100	50	100

Mean Dosage: Program 1.28 Units (S.D. .9)
Control 1.50 Units (S.D. .8)

Table IV
Anesthesia

Type	*Program* *No.*	*%*	*Control* *No.*	*%*
LOCAL				
A) Local alone	6	12	0	0
B) Local with whiffs of N_2O	20	40	15	30
Sub Total	26	52	15	30
CONDUCTION – Peridural	18	36	21	42
INHALATION				
A) Cyclopropane	4	8	2	4
B) N_2O & Cyclopropane	1	2	10	20
C) Local, N_2O & Cyclopropane	1	2	2	4
Sub Total	6	12	14	28
TOTAL	50	100	50	100

Table V summarizes the delivery technics employed with each group. A significantly higher percentage of prepared mothers had spontaneous deliveries (48% as compared to 26%). Moreover, in a larger number of controls (37 of 50), low forceps and other operative deliveries were necessary. In Thoms' series[11], 88.1% had spontaneous births, and 8.3% had vaginal operative deliveries. Other investigators report like results.[12, 19, 20]

As indicated by the findings listed in Table VI, there was no appreciable difference in the estimated blood loss. Thoms[11] reported that blood loss following delivery was less following the inauguration of the Prepared Childbirth Program. He attributed this to the relatively shorter labors and the decreased use of analgesic and anesthetic agents. Read[12] made this same conclusion. Laird and Hogan[18] found no significant difference in their controlled study.

Tables VII A, B, and C present the total labor and lengths of first and second stage, respectively. There were no apparent differences between the prepared and control patients. The longest individual labor in the prepared group was 26 hours, and in the control group, 22 hours. The shortest labor in the prepared group was 1 hour and 42 minutes; in the control group, 4 hours and 32 minutes. When considering primiparaa, Thoms[11] reported that 34% of the prepared patients had first stages lasting less than six hours, 63% ten hours or less, and 3% had labors exceeding 24 hours.

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*Demerol (Breon)
**Nisentil (Roche)

TABLE V

TYPE OF DELIVERY

	Program		Control	
Type of Delivery	*No.*	*%*	*No.*	*%*
Spontaneous Vertex	24	48	13	26
Low Forceps	18	36	26	52
Other Operative Procedures	8	16	11	22
TOTAL	50	100	50	100

TABLE VI

ESTIMATED BLOOD LOSS

	Program		Control	
Amount in cc.	*No.*	*%*	*No.*	*%*
200 or less	27	54	30	60
500 or less	20	40	18	36
800 or less	3	6	2	4
TOTAL	50	100	50	100

TABLE VII (A)

TOTAL LENGTH OF LABOR

	Program		Control	
Length in Hours	*No.*	*%*	*No.*	*%*
6 or less	7	14	10	20
12 or less	25	50	20	40
18 or less	11	22	15	30
26 or less	7	14	5	10
TOTAL	50	100	50	100

Average Length of Labor: Program 11 hrs. 7 min.
Control 11 hrs. 1 min.

TABLE VII (B)

LENGTH OF FIRST STAGE OF LABOR

	Program		Control	
Length in Hours	*No.*	*%*	*No.*	*%*
6 or less	13	26	12	24
12 or less	22	44	21	42
18 or less	10	20	15	30
26 or less	5	10	2	4
TOTAL	50	100	50	100

TABLE VII (C)

LENGTH OF SECOND STAGE OF LABOR

	Program		Control	
Length	*No.*	*%*	*No.*	*%*
30 min. or less	20	40	12	24
1 hour or less	19	38	22	44
2 hours or less	10	20	16	32
3 hours or less	1	2	0	0
TOTAL	50	100	50	100

Table VIII summarizes the Apgar ratings. It is noted that four times as many babies delivered among the controls had one-minute scores of 7 or less. Of these 12 control mothers, 7 had cyclopropane anesthesia, 3 had peridural, and 2 had N_2O and local anesthesia. There were no traumatic injuries, congenital anomalies, or infant deaths in the study. Thoms[11] felt that the number of depressed infants at birth was decreased. Tupper[14] reported that natural childbirth babies breathe and cry sooner, are less irritable, and have a diminished need for resuscitation.

The responses recorded on the obstetricians' postpartum questionnaire are reported in Table IX. Their impressions appear to indicate that management and satisfaction was facilitated by preparation for childbirth. Other investigators have reported excellent control of, and cooperation from their prepared patients.[12, 18, 19]

TABLE VIII

STANDARD APGAR RATINGS

	One Minute				Five Minute			
	Program		Control		Program		Control	
Apgar Scores	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0
2	0	0	1	2	0	0	1	2
3	0	0	2	4	0	0	0	0
4	0	0	2	4	0	0	0	0
5	0	0	0	0	0	0	0	0
6	1	2	3	6	0	0	1	2
7	2	4	4	8	0	0	0	0
Sub Total	3	6	12	24	0	0	2	4
8	11	22	6	12	0	0	4	8
9	29	58	26	52	8	16	11	22
10	7	14	6	12	42	84	33	66
Sub Total	47	94	38	76	50	100	48	96
TOTAL	50	100	50	100	50	100	50	100

Conclusions

Fifty private patient primiparas, who electively selected prepared childbirth training at the Yale-New Haven Medical Center, are compared with 50 private patient primiparas who had no program training. From this study, it is evident that:

1. Although a greater number of prepared patients required no analgesic medication, there was no significant difference in the average analgesic dosage between the two study groups.

2. A significantly higher percentage of prepared patients had local anesthesia, and a statistically greater number of unprepared patients had induction anesthesia. The number of epidural procedures, as well as the estimated blood loss, were approximately the same for each group.

TABLE IX

DOCTOR'S QUESTIONNAIRE

	Program						*Control*					
	Good		*Fair*		*Poor*		*Good*		*Fair*		*Poor*	
Factor	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Pain controlled	43	86	7	14	0	0	32	64	15	30	3	6
Patient Cooperative	50	100	0	0	0	0	36	72	13	26	1	2
Patient Satisfied	50	100	0	0	0	0	39	78	8	16	3	6

3. The lengths of the various stages of labor were not significantly different for the study groups. The average total length of labor for each group was slightly over 11 hours.

4. The control infants had a greater number of low Apgar scores than those delivered in the preparation program. A large percentage of the lower scores was associated with the administration of general anesthesia.

5. It was the impression of the attending private obstetricians that pain was better controlled, and patients were more cooperative and completely satisfied with their management in the prepared program.

6. The most important aspect of the Yale Prepared Childbirth Program appeared to be the support during labor, with the husband present during the first and second stages. The huge majority of prepared participants was satisfied with their experiences and indicated a desire to participate in childbirth training again.

7. The psychological benefits of prepared childbirth are obvious to the participating observer.

A further comparison of these program results with Thoms' series at Yale in 1954,[11] disclosed that the present number of "ideal", low analgesic, local anesthetic, spontaneous deliveries, was now less than previously reported for the Yale Prepared Childbirth Program.

Table X (A) briefly summarizes the responses to questions asked of the program trained mothers after delivery. It is noted that 2 mothers felt that the program was worthwhile, but would not select preparation again. One of these patients felt that she would perhaps feel the same without the program, while the other stated she would be satisfied with peridural anesthesia for future pregnancies. On the other hand, 2 mothers were indifferent toward the value of the program, but claimed they would try preparation again. One of these patients had a difficult delivery in which exercises did not help, while the other had a prolonged labor with considerable pain. Finally, 3 mothers were not satisfied with their experiences, but agreed to participate again. The first of these patients was not helped by breathing and exercises and did not see the birth of her baby. A second felt that childbirth was an individual and not a group problem, and that she did not learn enough from the classes. The last mother complained that her private doctor was not available when she needed him. In two reported series, 95% of the patients stated they would select training again.[17, 20] Other investigators report that 90% felt that preparation was successful and worthwhile.[14, 18]

Table X (B) presents the choices, as selected by the prepared group, for the most important aspects of the training program. The questionnaire response indicate that the support during labor, with the presence of the husband, as well as the instruction in the mothers classes, are significant contributions of the Yale program.

TABLE X (A)

PREPARED MOTHER'S QUESTIONNAIRE

	Yes		*No*		*Indifferent*	
Factor	*No.*	*%*	*No.*	*%*	*No.*	*%*
Satisfied with experience	45	90	3	6	2	4
Selection of program again	48	96	1	2	1	2

TABLE X (B)

PREPARED MOTHER'S QUESTIONNAIRE

Ranking of Importance	*1st Choice*		*2nd Choice*		*3rd Choice*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Mothers and Parents Classes	10	20	10	20	21	42
Exercises	4	8	6	12	10	20
Support during Labor	5	10	15	30	10	20
Husband's Presence during Labor	26	52	13	26	4	8
Doctor's Office Consultation	5	10	6	12	5	10
TOTAL	50	100	50	100	50	100

Several mothers commented that the awareness of what was going to happen helped to relieve the fears, frustrations, and mysteries of labor and delivery, making it possible for a more relaxed and cooperative approach. Furthermore, the interest and encouragement of the doctors, nurses, and particularly, the husbands, helped to give the mothers more confidence and a sense of security. One mother remarked, "To be awake at your baby's birth seems like the best way to begin your lives together." Another participant maintained that "preparation for labor and delivery is the best way to realize the excitement and fuller satisfaction of childbirth."

Commentary

Buxton[21] has sighted the need for continual objective evaluation, if possible, of the prepared childbirth program—both psychological and medical—in light of the numerous, difficult to measure intangibles. The mother's attitude toward children, her readiness for pregnancy, her whole life situation, certainly contribute to her particular management. Moreover, a self-selection basis of acceptance of patients in the program perhaps fosters assurance of the mother's cooperation and dedication. Admittedly, some patients can yield to psychological pressures to carry out their labors as the group intends. Such psychological reactions are highly individual and definitive measurements and conclusions cannot be made easily.

With these considerations in mind, one can comment on the outcome of this small sample survey. It is interesting to note that wives of university students and professional people comprised a large segment of the prepared population. This goes along with the contention that the greatest enthusiasm for natural childbirth is found among young, intelligent women, with wanted pregnancies, who are capable of understanding medical and psychological situations, and are able to comprehend the reasons for fear, and thus to help overcome them.

All prepared and control patients had private office visits with their obstetricians, where indoctrinations were directed toward the prevention of over-anxiety and panic in pregnancy, labor and delivery. These sessions are undoubtedly useful and valuable in establishing confidence and rapport with the physicians. At labor and delivery, however, only the program trained patients received full support by the hospital staff and the senior author. The program mothers were more enthusiastic and well-informed about the childbirth process. Furthermore, they appeared to be more confident and relaxed, and therefore were fully cooperative in their management. In general, the psychological benefits of the program were most evident to an attending observer of the labor, delivery and postpartum course of a prepared patient. Their enthusiasm and praise were magnanimous.

The physical benefits, on the other hand, are not as striking as they appeared to Thoms[11] ten years ago at Yale. Although the program trained mothers had less general anesthesia, and more spontaneous deliveries, these relative differences were not of the same magnitude as those previously reported by Thoms.[11] Moreover, there were no significant differences in the length of labor, estimated blood loss, or the amount of analgesic medication. The reasons for this apparent change in the past decade are not immediately apparent.

Of interest and unquestionable importance, however, were the significant differences in Apgar scores between the prepared and control groups. One is also impressed by the number of lower ratings associated with the administration of general anesthesia.

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Acknowledgements

The authors wish to express their gratitude for the great help received from Miss Ann Parsons, Class Instructor, and to Mrs. Myrtle Lippincott, Secretary of the Prepared Childbirth Program at the Yale-New Haven Hospital.

IMPORTANT! PLEASE READ!

CSMS Relative Value Coding on Third Party Payment Claim Forms

Pursuant to a request (regulation) of the State Department of Welfare that a "Relative Value Index No." be listed for each service for which claim is made for payment under Medicaid (Title XIX), the Council has voted to recommend to all members of the Society "that they use the CSMS Relative Value Studies coding and descriptions of services in making claims for payment from third party agencies, whenever requested to do so by such agencies."

The "Relative Value Index No." referred to on the Welfare Department's new claim forms (effective January 1, 1968) is that of the 1964 California Relative Value Studies, which, with minor amendments, was adopted as the official Relative Value Schedule of the Connecticut State Medical Society by the House of Delegates on April 27, 1965. Copies of the official CSMS Schedule were mailed to all current members in July of 1965, and a copy has been sent to each new member who has joined since that time, without charge. Additional or replacement copies may be obtained from the Society's headquarters office at the actual cost price of $2.50.

Family Planning Clinics In Connecticut

C. Lee Buxton, M.D.

Two and one-half years ago the 1879 Connecticut Contraceptive Law was nullified by United States Supreme Court decision thereby making the administration, sale, and use of contraceptives legally permissible in the State of Connecticut.

Previous to this any patient who could pay a private physician's fee could easily, and usually did, obtain appropriate contraceptive advice in a physician's office. The law had been economically discriminatory in a vicious way because public or semi-public institutions could not take the risk of openly violating the law by the establishment of contraceptive or family planning clinics. Thus the indigent patient, whether she was on welfare or otherwise, did not have this service available. From a socioeconomic point of view the very group where contraception was needed most, i.e. the indigent or medically indigent family, was deprived of a vitally important aspect of medical care.

Now that legal shackles have been removed, hospitals and other charitable institutions serving the indigent population are legally free to establish appropriate clinics and the population is free to attend them.

Are these institutions now availing themselves of this opportunity for service and is the population in question taking advantage of it?

In an attempt to find an answer to these questions, hospitals and other institutions in the State of Connecticut were sent questionnaires to find if they had established clinics, and if so, they were requested to answer various details of their clinic activity. It was assumed that only hospitals having an obstetrical service would be likely to have established contraceptive or family planning clinics. There are 34 such hospitals in the State of Connecticut delivering approximately 50,000 patients yearly. Their answers to the questionnaire were interesting. Some hospitals established contraceptive clinics immediately following nullification of the Law. One hospital stated that it had had a family planning clinic in operation for six years before the Law was repealed! Other hospitals had established clinics only recently. A total of 14 hospitals stated that they were serving their communities in this fashion. As to why the other hospitals had not established clinics there were no satisfactory standard answers. One hospital stated that the local environment was averse to the establishment of this type of clinic. Several others where the obstetrical service was largely on a private basis stated that patients desiring contraceptive care were referred to their private physicians. For the most part however the question of failure to establish a family planning center was left unanswered. This reluctance to establish a clinic may in some cases have been due to religious restrictions. However, two of the largest Catholic hospitals in the State have active family planning clinics at which they instruct husbands and wives in the technique of rhythm contraception; and a third is planning to have one. Their technique, carried out in association with the National Family Planning Association, involves extensive family cooperation and is based on the so-called "sympto-thermic" method used elsewhere in this country and especially in Canada and introduced into these Connecticut communities by Lanctôt.

In addition to hospital clinics the Planned Parenthood League of Connecticut has established six family planning centers in the larger cities of Connecticut and nine local Leagues have referral centers where pertinent information and literature can be obtained and referrals to various clinics made.

It has been estimated that there are in Connecticut 40,000 married women in the childbearing age whose economic status is considered to be medically indigent. However only ten per cent of these women are presently on welfare roles. The State Department of Welfare has been authorized to reimburse patients on welfare roles for the cost of obtaining contraceptive advice and materials, either from a clinic or from a private physician; but since such a small percentage of patients are enrolled as welfare patients there is a large number of indigent women desiring and needing contraceptive advice who cannot afford to obtain same except on a charitable basis.

DR. C. LEE BUXTON, Chairman Medical Advisory Committee of PPL Conn. and Professor of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Connecticut.

This is reflected in the number of patients applying to various different hospital and organizational contraceptive clinics for appropriate care. The hospital clinics have a patient attendance which varies from 3 to 40 new patients per week, depending to a certain extent on how long they have been in existence. An extrapolation of these figures to make an estimate of the number of new patients seen per year amounts to 6400. In addition to this the Planned Parenthood Centers over the past year have seen approximately 2000 new and old patients. Since only one of these Centers has been open for the entire year just passed, and two only recently established, the number in the future will presumably be much greater if this organization continues on its present program. This future probability of increased patient load is undoubtedly true of most of the hospitals clinics also. But it is apparent that there is a residue of thousands of women in Connecticut needing contraceptive care who are not receiving it. This is due partially to ignorance, partially to inertia, and partially due to the fact that a fee is charged for clinic care in these cases just as it is to any other cases who apply to clinics for medical care. The Planned Parenthood Centers charge a fee only if a patient can afford to pay it.

There are as yet no State, County or Municipal family planning clinics established. The State Legislature has not seen fit as yet to cope with this great social problem. However the New Board of Health is now hoping to establish satellite centers or clinics in the poorer economic areas of the City which will closely cooperate with the Family Planning Clinic of the Department of Obstetrics and Gynecology of the Yale-New Haven Medical Center and this may be the case in other cities also.

It is interesting to note the type of contraceptive advice which is administered to patients, both in the various hospital clinics and in the Planned Parenthood Centers. The "pill" is the most popular technique advised, 60.5% of patients being so treated in the former, and 54% in the latter clinics. Nine per cent are fitted with IUDs in hospital clinics and 19.9% in Planned Parenthood League Centers. Information on the type of IUD was not available in the former group, but in the Planned Parenthood League Centers the Lippes loop was used almost exclusively. In the hospital clinics rhythm contraception is administered to 14%. This figure is undoubtedly in actuality higher because one of the large Catholic hospitals has not as yet compiled their statistics. Patients in Planned Parenthood Centers who request rhythm contraception are referred to appropriate sources, mainly so that they can be put in contact with family group plans.

The diaphragm is prescribed for approximately 12-18% of patients in both groups, condom and other contraceptive techniques only rarely.

As will be seen, the total number of patients in Connecticut given contraceptive advice over a year's period is estimated to be about 8400 at the present time. This is a small number compared to the estimated 40,000 indigent married women of childbearing age for whom these services are available. Even on the reduced financial scale of a clinic the cost of these services is still prohibitive for a large number of women who are not necessarily on welfare roles. Presumably the facilities of various hospital planning clinics are not strained at the moment and could be enlarged should a means be found either locally or on a State basis for financing them. This is also true of the Planned Parenthood Centers which could be expanded both in size and numbers were financial resources available.

In addition to the administration of contraceptive advice and materials, all the Planned Parenthood Centers and most of the hospital clinics carry out a breast examination, complete pelvic examination, and Papanicolaou smear on each patient. Only one of the hospital clinics does not routinely do a Pap smear. This in itself is a valuable public health contribution and should significantly affect the incidence of early diagnosis of gynecological cancer.

This then, is an indication of the progress made in this field in Connecticut in the past two years. Progress on a large scale involving population groups inevitably has to overcome inertia, lack of information and both private and civil awareness of the necessity of financial support. The number of available family planning clinics as well as the patient population in each is rapidly increasing however. This kind of social and medical service may be said, therefore, to be playing an increasingly important role in the health and welfare of the population of Connecticut.

Summary

The number of contraceptive and family planning clinics established in the State of Connecticut since the nullification of the State Contraceptive Law has been reviewed.

Of the 34 hospitals in the State having an Obstetrical Service, 14 have established Contraceptive Clinics.

During the last two years the Planned Parenthood League of Connecticut has established six family planning centers and nine local leagues have information centers from which patients are referred to Contraceptive Clinics.

About 8400 patients are estimated to have been seen for family planning advice and treatment in the past year.

TYPE OF CONTRACEPTIVE ADVICE

	PPL Centers	*Hospital Clinics*
Oral Steroids	60.5%	54%
IUD	19.9%	9%
Rhythm	—	14%
Other	19.6%	23%

The various types of advised contraceptives have been reviewed.

It is estimated that there are about 40,000 medically indigent married women in the childbearing age for whom contraceptive advice should be available.

In order to make present and future Family Planning Clinics effective considerably more State, Municipal, and private financial aid must be provided for various family planning clinics.

Means must be found in presently existing and future hospital family planning clinics to make patients aware that such a facility exists and that services may be provided for little or no cost to the patient.

Closer cooperation between State and Municipal Welfare Agencies and various hospital Public Health facilities are needed to facilitate family planning consultations.

Commentary

In general practice I believe the art of history taking is different from that which is taught and used at hospital. In hospital a high percentage of cases are already diagnosed and organic in nature and the full picture is elicited by traditional methods, but in practice where I think the majority of cases are reactions of people to the life situation in which they find themselves, we must observe how these reactions present as symptoms. It is more effective to listen to a patient until he dries up, by which time the situational diagnosis is often clear. Asking questions interrupts the patient's natural flow of thoughts and words, often prevents an emotional catharsis and may keep the diagnosis at a superficial level. Whenever you feel uneasy about a patient, always look for depression and suicidal feelings and try to avoid involvement in their problems. *Aphorism*—Hospitals treat the disease behind the symptoms; general practitioners treat the situation behind the symptoms.—Ryde, D.: The Enigma of General Practice, *J Roy Coll Gen Practit* 14:132 (July) 1967.

FROM THE GENERAL MANAGER'S OFFICE

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CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1968 Annual Meeting of the House of Delegates will be held in the Terrace Room of the Hartford Hilton Hotel, Hartford. The first session of the House of Delegates will commence at 9:00 o'clock in the morning of Tuesday, April 30. Following luncheon, reference committee hearings will be held. The final session will commence at 3:30 o'clock in the afternoon of Wednesday, May 1.

E. Tremain Bradley, President
Kenneth F. Brandon, Speaker of the House
Charles Polivy, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider rsolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the Bylaws were presented to the House of Delegates on December 13, 1967 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

(PER DIRECTIVES OF HOUSE OF DELEGATES APRIL 25, 1967)
PREPARED AND APPROVED BY THE COUNCIL

I. Committee on Publications

Purpose: To abolish the Committee on Publications

Amendment

ARTICLE XI—Divisional Boards and Committees
Section 3. Divisional Standing Committees
  (D) Publications Division
    Delete the words "Committee on Publications"
Section 5. Duties of Standing Committees
  Par. 14 Committee on Publications
    Delete the entire paragraph
Renumber the succeeding paragraphs appropriately

II. Committee on AMA-ERF

Purpose: To abolish the Committee on AMA-Education and Research Foundation

Amendment

ARTICLE XI—Divisional Boards and Committees
Section 3. Divisional Standing Committees
  (A) Education and Hospitals Division
    Delete the words "Connecticut Committee on American Medical Education Foundation" (now called Committee on AMA-ERF)
Section 5. Duties of Standing Committees
  Par. 8 Connecticut Committee on American Medical Education Foundation (AMA-ERF)
    Delete the entire paragraph
Renumber the succeeding paragraphs appropriately

in moderate hypertension and poorly controlled mild hypertension

(when diuretics or sedatives are inadequate, for example)

When your patients expect a lot...

like relief from hypertensive symptoms
(headache, fatigue, nervousness, palpitation or insomnia, for example)

like an up-to-date, once-a-day dosage schedule
(a schedule not unlike timed-release medication, for example)

like a daily dose of medication for peanuts
(at 10¢ a tablet, for example)

like generally well-tolerated therapy
(as described in the package insert, for example)

...give them a little
(one tablet daily)

Regroton®
chlorthalidone 50 mg., reserpine 0.25 mg.

Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Regroton should be used in pregnant patients or in women of childbearing potential only when, in the judgment of a physician, its use is deemed essential to the welfare of the patients; adverse reactions (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn.
Precautions: Antihypertensive therapy with Regroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue Regroton therapy two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Regroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angiitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. (B) 46-600-B
For details, see complete Prescribing Information.

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Geigy

III. Advisory Committee to State Commissioners of Welfare, Finance and Control

Purpose: To change the name of the committee to "Liaison Committee with the State Commissioner of Welfare"

Amendment

ARTICLE X—Committees of the Council

Section 3. Representatives and Advisors

Par. 1. Outline

On line 3, change to read: Liaison Committee with the State Commissioner of Welfare

Par. 4.

Delete entire paragraph and substitute therefore the following:

Par. 4. *Liaison Committee with the State Commissioner of Welfare*

The Council shall elect annually a Liaison Committee with the State Commissioner of Welfare, to consist of not less than five members and appoint the chairman thereof. The purpose of this Committee shall be to maintain continuing liaison with the commissioner of welfare, to foster and promote cooperative relations between the commissioner, employed state personnel and all members of the medical profession, and to make recommendations concerning all professional aspects of the medical care and hospitalization of the beneficiaries of state-operated medical assistance programs.

IV. Delegates to the Council of New England State Medical Societies

(*not* a directive of the House of Delegates)

Purpose: To conform with the new CNESMS bylaws, calling for six (6) delegates from each member organization, instead of the former three (3)

Amendment

ARTICLE X—Committees of the Council

Section 3. Representatives and Advisors

Par. 10. Delegates to the Council of New England State Medical Societies. Change the wording of the first sentence to read: "The Council shall elect annually six delegates to the Council of New England State Medical Societies and designate the chairman thereof." The balance of the paragraph will remain unaltered.

V. Committee on Postgraduate Education

(*not* a directive of the House of Delegates)

Purpose: To make it *not mandatory* that a Clinical Congress be arranged and conducted annually. This would not preclude the Committee on Postgraduate Education from conducting future Clinical Congresses, if it were felt desirable to do so.

Amendment

Article XI—Divisional Boards and Committees

Section 3—Duties of Standing Committees

Delete the underlined words in the following paragraph:

Par. 6. Committee on Postgraduate Education. The Council annually shall nominate to the House of Delegates a Committee on Postgraduate Education to consist of not less than seven members and nominate the chairman thereof. The function of the committee shall be to plan and make available programs of postgraduate education for members of The Society, *TO ARRANGE AND CONDUCT THE CLINICAL CONGRESS OF THE SOCIETY,* and to cooperate with university and other agencies within the state for the extension of postgraduate education of physicians.

Delegates To Annual Meeting

The Bylaws of the Society provide that each county association is entitled to one delegate in the House of Delegates for each thirty-five Active or Life Members in the association or fraction thereof based on the membership as of December 31st of the immediately preceding year. According to this, the quota of delegates from each county association who should attend the Annual Meeting of the House of Delegates which will be held in Hartford, April 30, 1968, May 1, 1968, and the Semi-Annual Meeting in December, 1968 is as follows:

County	*Membership Dec. 31, 1967*	*Official Delegates*
Fairfield	978	28
Hartford	1128	33
Litchfield	147	5
Middlesex	118	4
New Haven	1029	30
New London	212	7
Tolland	29	1
Windham	74	3

Election Of Councilors and Associate Councilors

Councilors and Associate Councilors, who shall serve for two years, shall be elected this year at the annual meeting of each of the county associations in Fairfield, Litchfield, New Haven and Tolland counties. In accordance with the Bylaws, each component association having over 750 members may elect one additional Associate Councilor. Therefore, the Fairfield and New Haven Medical Associations should elect a Councilor and two Associate Councilors for a two year term.

No Councilor or Associate Councilor elected by a component association shall serve more than three successive terms of two years each in his respective office, but after a lapse of one term of two years, such Councilor or Associate Councilor shall be eligible for reelection.

Newly elected Councilors and Associate Councilors shall not assume office until after the Annual Meeting of the House of Delegates.

SUMMARY OF ACTIONS
COUNCIL MEETING
Wednesday, January 17, 1968

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Bradley, Gardner, Grendon, Brandon, Caplan, Fabro, Hess, Rogol, Abbot, Hastings, Ayres, Jacobson, Jr., Johnson, Petrie, Pelz, Wilson, Roch and Granoff. Also present were: Mrs. Lindquist, Mr. Norbeck (AMA) and Dr. Richards. Absent were: Drs. Polivy, Cramer, Egan, Spitz, Shepard, Nolan, Grant and Palomba.

II. ROUTINE BUSINESS

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Derick A. January, Hartford (HCMA)—1968
Irving J. Marshak, New Haven (NHCMA)—1968
Maxwell O. Phelps, Hartford (HCMA)—1968

Date of Next Meeting

The date of the next Council meeting is scheduled for Thursday, February 15, 1968, starting at 10:30 A.M. The meeting will be followed, in the afternoon of that day, by the Fourth Conference of County Medical Association Officers at the New Haven Lawn Club, New Haven, at 2:30 P.M.

III. OLD, NEW, AND SPECIAL BUSINESS

Election of Student Members

It was VOTED to elect to Student Membership two applicants as follows:

Lucienne A. Cahen, 225 Fountain Street, New Haven
  University of Maryland—1971
  Pre-Med: Sarah Lawrence College
  Parent: Raymond L. Cahen
Theodore W. Maron, Jr., M.D., 49 Woodland Park, Hartford
  New Jersey College of Medicine—Class of 1967
  Pre-Med: Tufts College
  Parent: Theodore W. Maron, Sr.

Reports of Fiscal Advisory Committee

Actions were taken on a series of recommendations of the Fiscal Advisory Committee as follows:

(a) *64th Annual Congress on Medical Education, Chicago, Feb. 9-12, 1968*: It was VOTED to authorize a member of the CSMS Committee on Medical Education and Licensure, Charles B. Cheney, New Haven, to attend this Congress as a representative of the Society, and to authorize his reimbursement for usual expenses in attending same in the amount of up to $250.

(b) *AMA 2nd National Congress on Socio-Economics of Health Care, Chicago, March 22-23, 1968*: It was VOTED to request the Chairman to designate a CSMS member to attend this Congress as a representative of the Society, and to authorize reimbursement of the member designated for usual expenses in attending same in the amount of approximately $200.

(c) *Regional Workshop on Medicine and Religion, New York, March 23, 1968*: It was VOTED to authorize reimbursement of transportation expenses of a CSMS representative attending this Workshop in the amount of approximately $20.

(d) *Connecticut Physicians Art Association Exhibit*: It was VOTED that the Society sponsor this exhibit as a function of the 1968 Annual Meeting, and contribute up to $200 to help defray expenses attendant to same out of General Funds.

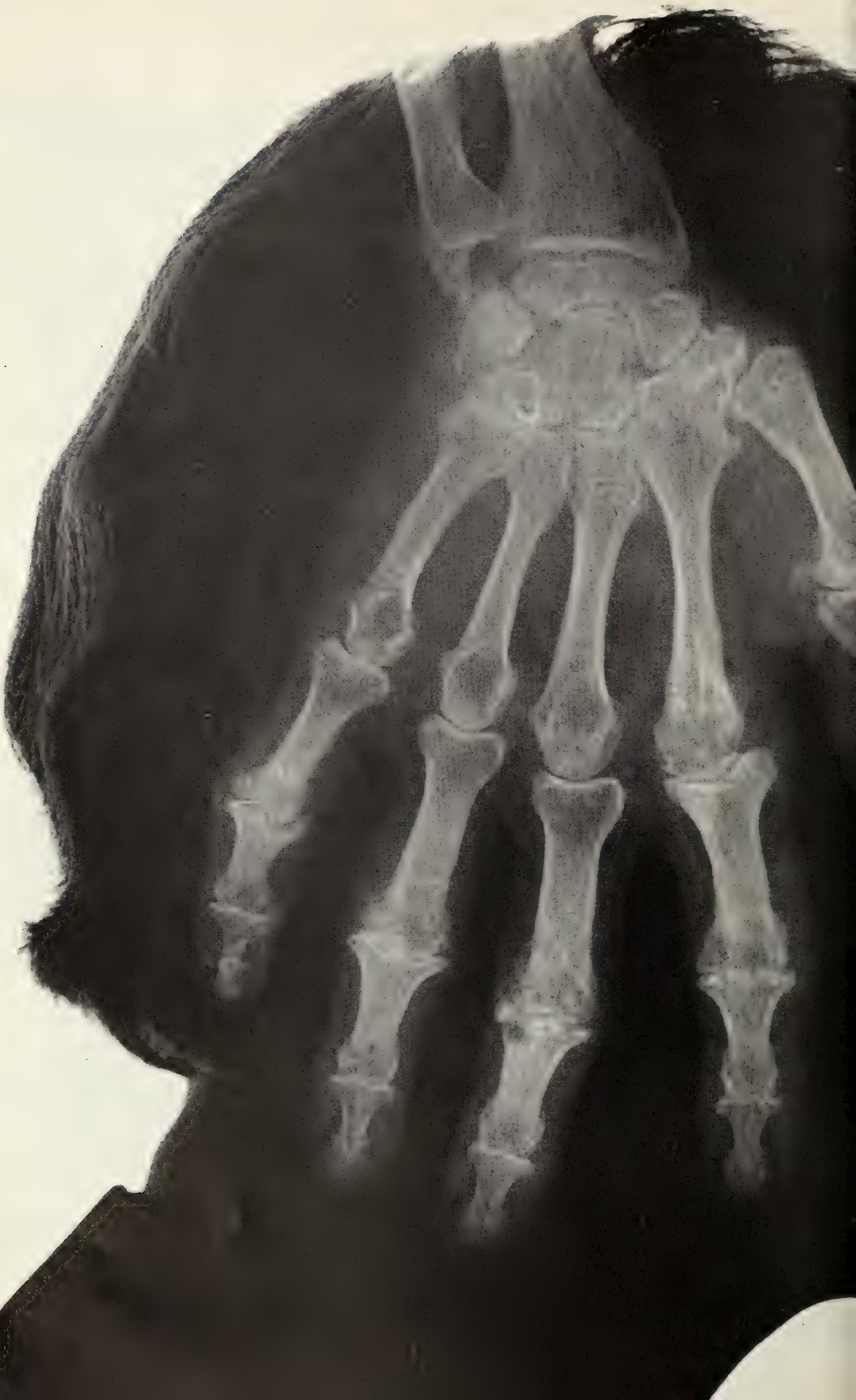
Resignation—Editorial Committee of Journal

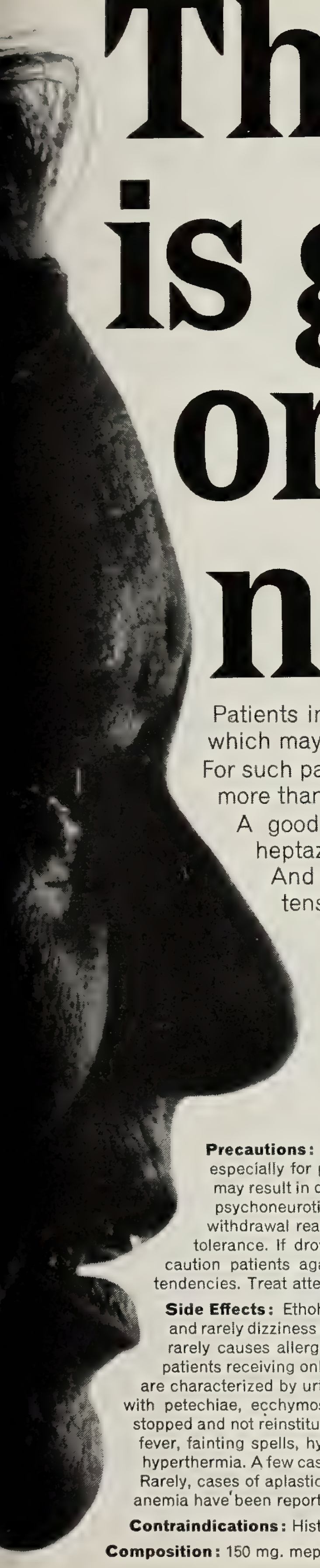
It was VOTED to accept, with regret, the resignation of Joseph L. Belsky, Danbury, as a member of the Editorial Committee of *Connecticut Medicine.*

Report—Committee on State Legislation

Actions on a four-part report of this Committee were taken as follows:

(a) *Legislative Counsel*: It was VOTED to approve the Committee's "job description" of a legislative agent to meet the Society's needs, and to authorize the Committee to seek to locate a person





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A good choice is often EQUAGESIC® (meprobamate and ethoheptazine citrate with aspirin). It helps relieve pain. And anxiety. And skeletal muscle spasm as related to pain or anxiety and tension.

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Precautions: Keep out of reach of children. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. Withdraw gradually after prolonged high dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance. If drowsiness, ataxia or visual disturbances occur, reduce dose. If symptoms persist, caution patients against operating machinery or driving. Give cautiously to patients with suicidal tendencies. Treat attempted suicide with immediate gastric lavage and appropriate supportive therapy.

Side Effects: Ethoheptazine and aspirin may occasionally cause nausea, vomiting, epigastric distress, and rarely dizziness and CNS depression. Overdosage may result in salicylate intoxication. Meprobamate rarely causes allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. Meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioedema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. A few cases of leukopenia, usually transient, have been reported following prolonged dosage. Rarely, cases of aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported; almost always, in the presence of known toxic agents.

Contraindications: History of sensitivity or severe intolerance to aspirin or meprobamate.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

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or persons having these qualifications and to make recommendations to the Council concerning engagement of same.

(b) *Contacts with Legislators*: It was VOTED to approve the Committee's proposal to arrange discussion meetings between representatives of pertinent committees of the Society and related committees of the General Assembly, and to approve the expenditure of up to $1500 for up to five dinner meetings for this purpose (at a per dinner meeting cost not to exceed $300).

(c) *Revising Connecticut's Abortion Statutes*: It was VOTED to receive as information a report on the progress being made toward formulating a policy with respect to "liberalizing" the abortion statutes to be presented for approval by the Council and/or House of Delegates.

(d) *Changes in Committee Composition*: It was VOTED to refer to the Council's Sub-committee to Study the Bylaws, for study and report, a recommendation of the Committee that the bylaws be amended to provide for broader-based composition of the Committee than presently exists.

Reports—Committee on Third Party Payments

Actions were taken on two reports submitted by this Committee as follows:

(a) *Updating the Relative Value Schedule*: Having been apprised by the Committee that certain difficulties (lack of cooperation) were being encountered in obtaining from participating CSMS Sections and allied groups recommendations concerning desired changes in the unit values of the RVS, and of the opinion of the Committee that perhaps the RVS was no longer of sufficient value or interest to members of the Society to be considered important, the Council VOTED to reaffirm its confidence that the Relative Value Schedule is of use and importance to the Society and its members (including its value for coding and providing descriptions of procedures) and to urge the Committee on Third Party Payments to continue to exert whatever effort is required to update the Schedule.

It was further VOTED to recommend to all members of the Society that they use the CSMS Relative Value Study coding and descriptions of procedures in making claims for payment from third party agencies, whenever requested to do so by such agencies (including Title XIX, Medicaid).

(b) *Relative Values of Physicians' Services in Extended Care Facilities*: Pursuant to several earlier requests of the Council, the Committee submitted a series of six "statements" concerning various types of physicians' services to patients in extended care facilities. It was VOTED to approve the series of statements, and to forward same to the Connecticut General Life Insurance Co. (carrier for Medicare B) with the request that CG be guided by them in making payments for such services and publish and distribute them to physicians in the state as policy information.

Communication—A. H. Robins Co. re Physician Award

It was VOTED to refer to the Public Relations Division, for study and report, a proposal by the A. H. Robins (Pharmaceutical) Co. that the Society consider making a "Physician Award" for outstanding community service, the award plaque being furnished by the Company without charge or participation in the selection of the physician to receive it.

Communication—Connecticut Society of American Board Obstetricians and Gynecologists

It was VOTED to receive as information, and with thanks, notice that the CSABOG has gone on record as "firmly adherent to the prevailing policy of usual and customary charges" and opposed "to any new third party fixed payment plan which would undermine this policy". Review of the CMS Century Contract led the CSABOG members to take this action, it was reported.

Communications re Hospital-Based Diploma Schools of Nursing

(a) It was VOTED to accept, with commendation, a report filed by Hilliard Spitz, Chairman of the Committee on Allied Medical Services, which presented background information on, and explanation of, the movement among national and state nursing organizations to "phase out" the hospital-based diploma schools of nursing in favor of the baccalaureate schools over a period of years (target date: 1976). Meanwhile, the nursing organizations favor the continuance of the diploma schools with maintenance and upgrading of educational quality. Their goal is to produce the same or greater numbers of baccalaureate nurses as are presently being produced by all sources, including diploma schools.

(b) It was VOTED to receive as information a report filed by J. Alfred Fabro, Torrington, on the proceedings of the AMA Conference on Nursing, Chicago, October 5-6, 1967, which he attended as a representative of the Society. In Dr. Fabro's opinion, the Society should take steps to urge the Governor to appoint a commission to study nursing needs in Connecticut and to make recommendations con-

Before prescribing, see complete prescribing information in SK&F literature or *PDR.* A brief precautionary statement follows.
Contraindications: Glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal obstruction, or bladder neck obstruction.
Precautions: Use cautiously in the presence of hypertension, hyperthyroidism, coronary artery disease; warn vehicle or machine operators of possible drowsiness.
Usage in Pregnancy: Use cautiously, especially in the first trimester. *Note:* The iodine in isopropamide iodide may alter PBI test results and will suppress I^{131} uptake; discontinue 'Ornade' one week before these tests.
Adverse Reactions: Drowsiness; excessive dryness of nose, throat or mouth; nervousness; insomnia. Other known possible side effects of the individual ingredients: nausea, vomiting, diarrhea, rash, dizziness, fatigue, tightness of chest, abdominal pain, irritability, tachycardia, headache, difficulty in urination. Thrombocytopenia, leukopenia and convulsions have been reported but no causal relationship has been established.

a stuffy nose
is no
laughing matter

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Each capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate), 50 mg. of phenylpropanolamine hydrochloride, and 2.5 mg. of isopropamide, as the iodide.

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give him all-day
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cerning what should be done to meet those needs, including recommendations concerning programs of nursing education. No specific action was taken on Dr. Fabro's suggestion.

Reconsideration—CSMS Policy on Laboratories and Physician-Laboratory Relations

An apparent conflict between two separate but related actions of the Council regarding these matters was brought to the attention of the Council by the Chairman and the General Manager. As a consequence, it was VOTED to reconsider the two actions in question. Pursuant to reconsideration, it was voted to reaffirm approval (11/16/67) of the report of the Committee on Preliminary Study of Censorship Questions on the subject of "Ethics of Contractural Arrangements Between Physicians and Clinical Laboratories" which stated (in essence) that such arrangements are ethical provided that: (a) the physician has assured himself of the quality and reliability of the services furnished by such a laboratory; (b) the physician passes on to his patients any savings which may accrue from such contractural arrangements; and (c) the physician does not profit financially from the arrangement and limits the source of his professional income to medical services rendered by him or under his personal supervision.

It was VOTED to rescind the Council's action of October 18, 1967 (on recommendations made by the Connecticut Society of Pathologists) and to substitute therefor the following:

That CSMS shall limit acceptance of clinical laboratories as exhibitors or advertisers to those which are licensed and supervised by the Connecticut State Department of Health, and to those out-of-state laboratories which satisfy the standards of the CSMS Committee on Public Health and/or the State Health Department as to the reliability and accuracy of the services offered in Connecticut.

Reports—Committee on Mental Health

On two matters referred to it by the Committee on Mental Health, the Council took the following actions:

(a) It was VOTED to amend, and approve as amended, a resolution introduced by the Committee which would seek from Connecticut Blue Cross an explanation of a recent Blue Cross action which reduces coverage for mental patients admitted to general hospitals from 90 days to only 30 days. Voicing the opinion that this reduction in coverage appeared to "discriminate" against the patient suffering from psychiatric illness, the resolution calls upon the Society to inquire of Blue Cross as to what facts and factors entered into the making of the subject decision.

(b) It was VOTED to refer to the Committee on National Legislation, the Conference Committee with the Connecticut Pharmaceutical Association, and the Delegates to the American Medical Association a resolution introduced by the Committee on Mental Health which called on the Society to "take action" which would promote the enactment of Federal legislation which would permit the telephone prescribing of Class A Narcotics, with a written prescription to follow (to the pharmacist) within twenty-four hours, and to request the National Legislative Committee, the Conference Committee with CPA, and the AMA Delegates to make recommendations to the Council as to what actions should be taken by the Society to implement this resolution.

Reports on AMA Planning Conference on Health Care for the Poor

It was VOTED to accept, with commendation, reports filed on the proceedings of this Conference (Chicago, December 15-16, 1967) by Norton G. Chaucer, Hartford, and Donn C. Barton, Portland, both of whom attended as representatives of the Society. Drs. Chaucer and Barton have been appointed co-chairmen of an Ad Hoc Committee on Health Care of the Poor in Connecticut, and the Chairman of the Council will shortly appoint additional members to the Ad Hoc Committee. Arrangements are being made to have representatives of CSMS meet with representatives of agencies working in poverty areas in major cities throughout the State to jointly review the Title XIX Medicaid program and discuss other matters having to do with the delivery of quality medical services to the residents of such areas.

Informational Report on "Tri-State Planning Agency"

The Council received an informational (but *not* detailed) report on a Federal grant that has been applied for by Connecticut's Commissioner of Finance and Control to establish a "Regional Health Resources and Information System for Coordinated Planning and Management" for the states of Connecticut, Rhode Island and Massachusetts. Submitted to the Public Health Service of the Department of Health, Education and Welfare in early September, 1967, the application was accompanied by supporting statements signed by the

Governors of the states concerned and a number of major commissioners.

Concluding that the voluminous descriptive document which accompanied the grant application was too complex and far-reaching for ready comprehension of its scope and significance, the Council was unable to form any opinions as to the merits of the proposed "Tri-State" plan itself. However, the Council expressed consternation that, as far as could be determined, none of the representative voluntary health agencies in any of the three states had been informed of the plan or that a grant application had been made to implement same. It was therefore VOTED to communicate with Governor Dempsey to inquire about the development of the plan without apparent consultation with any of the health agencies presently engaged in various activities related to such studies and planning, and to ask whether the content of the proposal had been considered by its authors to not be of interest to such agencies. Copies of the letter to be sent to State Commissioner of Health, Commissioner of Finance, Connecticut representatives in Congress, and U. S. Surgeon General.

Report—Advisory Committee to State Commissioners

(a) It was VOTED to receive as information a report filed by this Committee on the matters discussed with Commissioner Shapiro and his staff at a meeting on November 21, 1967. In brief, these matters were: Use of Specific Pharmacies (any pharmacy may be used except for patients in extended-care facilities); Dollar Limitations on Prescriptions (cost should not exceed $10 without authorization); Limitation on Type of Drugs (no limitations, except for items such as multivitamins, appetite depressants, etc.); Consultations (reasonable free choice by attending physician); and New Billing Form (new form to be used after March 1, 1968, for usual and customary charge method, presented and discussed).

(b) Dr. Bradley informed the Council that (via the telephone) Commissioner Shapiro has stated that since the Advisory Committee to the State Commissioners of Welfare, Finance and Control is no longer called for (under the Medicaid Statutes), he suggests that the Committee be abolished. Accordingly, it was VOTED to disband the Advisory Committee and to request the Subcommittee to Study and Revise the Bylaws to draft appropriate amendments to accomplish same. Notice of this action will be transmitted to Commissioner Shapiro, and he will be asked to confirm the fact that it is in accordance with his wishes.

Miscellaneous Actions

(a) Having learned of the death of the father of Hilliard Spitz, Councilor from NLCMA, it was VOTED to convey the condolences of the Council to Dr. Spitz on his bereavement.

(b) It was VOTED to convey a message of sincere thanks to the officers and members of the New London County Medical Association for the excellent facilities provided, and cordial hospitality extended, by the Association, to members of the House of Delegates at the meeting in Groton on December 13, 1967.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on January 17, 1968. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

OBS-GYN—Board Certified Ob-Gyn Fellow, Age 32, University trained, Military service recently completed. Seeks group or association practice.

SURGEON—37 years of age, Board eligible, Connecticut license. Wishes to associate with a group or another surgeon. Available immediately.

PATHOLOGIST—36 years of age, Board certified, Connecticut license. Interested in a group, associate or institutional practice and can be available within one month.

G.P.—34, currently completing military tour desires to locate in Connecticut. Four years' solo practice experience. Solo, association or group, emergency room, college health. Connecticut license. Available on or about March 1.

ALLERGIST—Board eligible internist with special interest in allergy wishes to locate in Connecticut. Connecticut license, presently completing military duty. Wishes to practice with a partner or in a group. Available about March 10, 1968.

G.P.—Applied for Connecticut license. Well trained in Anesthesiology and would like to practice with an associate or in a solo situation. Military obligations completed, available, March, 1968.

PLACEMENT OPPORTUNITIES

INTERNIST OR G.P. wanted in association leading to partnership with G.P. who has "quality" family practice. Do no surgery. Am associate attending at one hospital and courtesy staff at second. City of 175,000 in Connecticut. Phone 233-5554.

WANTED—Qualified family doctor to take over practice 30 minutes from Hartford. No obstetrics or orthopedics. Expense-sharing and coverage arrangements with M.D. in same office building. Nearby lab and x-ray. Low price for equipment. No charge for goodwill and introductions. Leaving to specialize. Contact: Lawrence S. Carlton, M.D., 65 Maple Avenue, Collinsville, Connecticut, Telephone 693-4017.

RADIOLOGIST to associate with 3 radiologists; expanding hospital and office practice in Hartford area; remuneration: negotiable, leading to full partnership. Contact Albert C. Hurwit, M.D., 477 Connecticut Boulevard, East Hartford, Connecticut 06108.

ESTABLISHED PEDIATRICS PRACTICE available. New owner to buy present owner's equipment and share of office building. Terms of sale negotiable. Short distance from new medical school, excellent local hospital.

SENIOR STAFF PSYCHIATRIST, full time, residential rehabilitation center 40 miles from New York, in desirable living area with good schools. Non-profit organization oriented to intensive, individualized eclectic psychotherapy. Large outpatient service also. Salary open dependent on experience. Benefits include major medical insurance, life insurance and pension program. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut, 06840.

PHYSICIANS needed for full-time work in Masonic Home and Hospital, Wallingford, Connecticut. High salary, excellent benefits, good working atmosphere.

HOUSE PHYSICIAN—Diversified duties in voluntary, accredited hospital. Connecticut license required. 45 hours a week, Monday through Friday; no weekends. Immediate placement. $18,000 a year. Write P. O. Box 3474, Bridgeport, Conn. 06604.

NEWLY APPROVED 3 YR. RESIDENCY now offered at Hartford Hospital with combined clinical experience at Newington Hospital for Crippled Children and The Gaylord Hospital. Teaching affiliation with Yale-New Haven Medical Center. Supervision under full-time psychiatrists. Experience available in a variety of child and adult disorders. Write Carl V. Granger, M.D., Hartford Hospital CCU1, 80 Seymour Street, Hartford, Connecticut 06115.

WANTED: Internist, Board eligible, to associate with two busy young internists in modern spacious offices in a New Haven suburb. Excellent hospital facilities available. A fine opportunity for rapid growth. For further information contact: Marvin P. Zimmerman, M.D., or Edward S. Scherr, M.D., 960 Main Street, Branford, Connecticut 06405.

NEW YORK State Narcotic Addiction Control Commission has full or part-time openings to provide psychiatric services for resident addicts in rehabilitation centers in the Mid-Hudson River Valley area (Woodbourne, Beacon, Stormville, New York). Exceptional opportunity to supplement private practice in areas with minimal psychiatric coverage, or to begin long-range association with dynamic, challenging, total approach rehabilitation program. Bd. Cert. or Elgbl. Write Assistant Commissioner—S. Seymour Joseph, M.D.—Dept. P-24, 1855 Broadway, New York, New York 10023.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Doctor's Office

Arthur A. Echental, M.D., announces the opening of an office specializing in the diseases of the skin at 98 Hoyt Street, Stamford.

Herbert Gold, M.D., announces his association with Malcolm S. Roth, M.D. for the practice of ophthalmology at 100 Constitution Plaza, Hartford.

J. William Healy, M.D., announces the opening of an office for the practice of neurology at 51 Gillett Street, Hartford.

Robert Kinstlinger, M.D., announces the opening of an office for the practice of internal medicine at the West Haven Professional Building, 385 Main Street, West Haven.

Bernard Klein, M.D., announces his association with Robert F. McGann, M.D. for the general practice of medicine at 244 Main Street, South Meriden.

Henry C. Rogers, M.D., announces the opening of an office for the practice of internal medicine at 81 South Main Street, West Hartford.

Donald Wallace, M.D., announces the opening of an office for the general practice of medicine at 26 Fair Street, Wallingford.

a tranquilizer with particular usefulness in functional disorders

Tybatran™

(pronounced TYE-buh-tran)

brand of tybamate

Extensive clinical experience, including eleven double-blind studies,[1-11] indicates that Tybatran is an effective agent for the relief of anxiety and tension. It appears to lend itself particularly well to the management of the anxious patient who "somatizes"—whose anxiety and tension find expression in complaints such as headaches,[4,8,10,11] fatigue,[4] insomnia,[2,4,8,9,12] anorexia,[3,8,9] and pruritus.[7]

Two salient features seem to set Tybatran somewhat apart from certain other commonly used tranquilizers.

1. Tybatran often proves more effective than meprobamate and chlordiazepoxide. In one study,[4] severe anxiety responded more effectively to tybamate than to meprobamate; in another,[8] symptom-response superiority of tybamate over chlordiazepoxide was marked at statistically significant levels of confidence.

2. Tybatran appears to be less sedating than other widely used tranquilizers. Side reactions are relatively infrequent; when they do occur, they may take the form of drowsiness, although insomnia, ataxia and other adverse effects have been reported. Nevertheless, Tybatran impresses many clinicians by its comparative lack of undesirable sedative action.[3,6,12,13] (If drowsiness or vertigo is present, activities requiring optimal alertness should be avoided.)

For patients in whom anxiety is manifested in any of a multiplicity of physical complaints, Tybatran deserves a clinical trial. These are the challenging patients, those with recurrent, persistent, ever-changing symptoms for which there is no clinical or laboratory evidence of organic disease.

Usual adult dose: one or two 250 mg. capsules 3 or 4 times daily. Adjust to suit individual requirements.

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Prescribing Information

Dosage and administration. The suggested adult dose of Tybatran (tybamate) is one or two 250 mg. capsules three or four times daily. Dosage should be adjusted to suit individual requirements. While clinical experience with Tybatran (tybamate) in children has been very limited to date, the recommended daily dosage for children 6 to 12 years old is 20 to 35 mg./kg. body weight, in three or four equally divided doses. Dosage should be adjusted to suit individual requirements. Until further clinical experience is obtained, administration of Tybatran (tybamate) to children under 6 years of age is not recommended. Daily doses larger than 3000 mg. are not recommended, although in a few instances doses in excess of this figure have been administered. Tybatran (tybamate) is also available in 350 mg. capsules, for convenience in dosage adjustment, e.g., one capsule three times daily and two at bedtime.

Contraindications. Tybatran (tybamate) should not be administered to patients known to be hypersensitive to the drug. Since no studies have been done with this drug in human pregnancy, it should not be used in pregnancy unless the potential benefit outweighs the risk.

Warnings. Simultaneous administration to psychotic patients of tybamate with phenothiazines and other central nervous system depressants has in a few instances been associated with the occurrence of grand mal or petit mal seizures. Seizures have been reported with administration of phenothiazines alone, but not with administration of tybamate alone; nevertheless, tybamate should be used cautiously in individuals who are receiving other central nervous system depressants or have a history of convulsive seizures. Also, it should be borne in mind that simultaneous administration of tybamate with alcohol or with other psychotropic agents, particularly phenothiazines or monoamine oxidase inhibitors, which are known to potentiate the action of other drugs, may result in additive actions.

Precautions. There has been no evidence to date of the development of habituation or addiction. Investigators have not observed excessive self-medication or any withdrawal symptoms with use of Tybatran (tybamate), but the latter should be kept in mind with cessation of the drug after prolonged use. Because of the occurrence of

Prescribing information continued on next page.

(pronounced TYE-buh-tran)

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Prescribing information continued from preceding page.

withdrawal symptoms or exacerbation of presenting symptoms upon rapid withdrawal of other agents of this type, abrupt withdrawal of Tybatran (tybamate) should be avoided. Tybamate, like other psychotherapeutic agents, should be used with caution in addiction-prone individuals. Should symptoms of hypersensitivity occur, administration should be discontinued at once and appropriate symptomatic treatment initiated. Operation of motor vehicles or machinery or other activities requiring optimal mental alertness should be avoided if drowsiness or vertigo is present. As with any new drug, Tybatran (tybamate), should be used with caution in patients with a history of drug allergies, blood dyscrasias, and hepatic or renal disease; and prolonged and/or high doses of tybamate should be accompanied by periodic measurements of hepatic, hematopoietic, and renal function.

Adverse reactions. While these have only rarely required discontinuation of the drug, the most frequently encountered reactions have included drowsiness, dizziness, nausea, insomnia, euphoria. The drug was discontinued in one child because of a possible drug-induced urticaria, and skin rash and pruritus have been encountered in a few other patients. In a few patients, effects suggesting excessive stimulation such as hyperactivity, fidgetiness, flushing, and tachycardia have been encountered. Other reported side effects recorded only a few times to date have included ataxia, unsteadiness, confusion, feeling of unreality, "panic reaction," fatigue, headache, paresthesias, vertigo, gastrointestinal disturbances, glossitis and dry mouth. Grand mal or petit mal seizures have been reported in a few hospitalized psychotic patients to whom tybamate (up to 6000 mg. daily), phenothiazines, and other psychotropic agents were administered simultaneously. Convulsive seizures have not been reported with the use of tybamate alone.

Until clinical experience has accumulated with this drug, inasmuch as tybamate is related to meprobamate, the physician should be cautious about the possibility of rare, serious adverse reactions such as may be encountered with the latter drug. Should excessive doses of tybamate be ingested, it is recommended that any drug remaining in the stomach be removed and symptomatic therapy, including central stimulants, be used as necessary.

Supply. Tybatran (tybamate) is available in green, sealed capsules of three strengths: 350 mg., 250 mg., and 125 mg. Each strength is supplied in bottles of 100 and 500.

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CAUSES OF CHILDREN'S DEAFNESS CHANGING

The causes of children's deafness are changing fairly rapidly, reports a medical journal published by the American Medical Association.

"Acquired" deafness due to infection, injury, etc., is declining, partly because of effective antibiotics and other medical treatment.

On the increase, however, is congenital deafness caused by premature births, German measles infection of pregnant mothers, and incompatibility of the Rh factor in the mother's and child's blood.

Of these, premature birth is of increasing importance, primarily because more premature babies are surviving.

Prematurity causes other disabilities in addition to deafness. In the future, schools of the deaf will be dealing with more of these complications "which may interfere with training the hard of hearing," the report said.

When two investigators surveyed admission records of the Pennsylvania School for the Deaf in 1960-61 and again in 1964-65, they found noteworthy changes in the distribution of kinds of deafness.

There was a doubling of cases of "congenital, nonhereditary" deafness—mostly due to prematurity—in the four years between surveys.

Deafness due to infections and illness was almost cut in half during this same period. The authors attribute much of this decline to increasing use of antibiotics to combat these infections.

Almost unchanged, however, was the percentage of cases due to viral infections unaffected by antibiotics.

The effects of Rh incompatibility reached a peak in children born between 1949 and 1951, and declined thereafter. This may coincide with better recognition, treatment, and survival of these children, the authors said.

Authors are Jacob M. Danish, M.D. and Max Levitan, Ph.D., of the Woman's Medical College of Pennsylvania, Philadelphia. Dr. Levitan is now at George Mason College of the University of Virginia, Fairfax, Va.

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THE ETHICS OF MEDICAL CREDIT CARDS

Since it appears that, in the near future, medical credit or bank cards will be offered to the public as an innovation in the field of financing health care costs, the following is published for the information of the membership:

OPINION OF THE AMA JUDICIAL COUNCIL

November 26, 1966

Participation by Physicians in Bank Card Programs

The growth and development of credit cards is burgeoning. A new form of card, the so-called *bank card,* is being widely introduced. Bank cards are issued without cost to the cardholder; they are acceptable at many places than conventional credit cards; they are sponsored by large, reputable banks. They are an innovation in our economic system.

As these bank card plans have come into being, in all parts of the country, physicians have asked if they may ethically use bank cards as a form of payment for professional services. Some medical societies have said physicians may participate; others have said physicians may not.

The Judicial Council believes a uniformity of opinion is desirable. In matters of ethics it would seem indisputable that a general rule should be determined for the guidance of the profession, and that this rule should be implemented at local level.

The medical profession has officially recognized that it cannot dictate to patients how they shall finance their medical bills. It can and should, however, determine principles to guide its members in determining whether and how they may participate in any payment program.

If the bank card were merely a substitute for cash or check in the payment of bills, little or no problem would be presented to physicians regarding their use; they would be merely a newly adopted medium of exchange. Bank cards, however, serve a twofold function: They are a convenience—a substitute for currency or check in the payment of indebtedness; and they are also a financing mechanism. Consequently, their indiscriminate use, especially the financing of larger medical bills through banks, could result in additional cost to patients. While the doctor's fee for medical care would not increase, the cost of financing payment of that fee through a third party would be imposed on the patient. Of course, patients may voluntarily elect to pay larger amounts in return for the convenience of a given program. Still, the medical profession has a responsibility to guard against patients being placed in untenable financial conditions because of overall medical care costs. That is why medicine has been in the forefront in encouraging prepayment and insurance programs to provide for the costs of medical services. It must, therefore, maintain its position of safeguarding patients interests when considering new methods of financing personal indebtedness.

The Judicial Council is of the opinion that neither endorsement nor disapproval should be given to the bank card system at this time.

In June, 1965, the Judicial Council and the Council on Medical Service jointly agreed that any proposed plan for financing medical care or parts of medical care should be judged by the physician in the light of whether or not it might "result in advertising or solicitation of patients by physicians, profit to physicians for other than professional service, exploitation of the patient, or unnecessary increase in the cost of medical care."

Judged by these criteria, the Judicial Council is of the opinion, at this time, that physician participation in bank card programs is not per se unethical. It is of the opinion that physicians may ethically accept bank cards in the payment of current medical bills in lieu of cash or check, that is, as a medium of exchange.

The use of bank cards in financing medical fees must, however, be viewed with reserve at the present stage of their development. While patients may not be denied the right to determine matters of their personal budgeting, physicians must not encourage the use of this financing method if in operation it might compromise the ideals of the medical profession or add to the financial burden of patients.

In connection with physician participation in bank card programs, the Judicial Council recommends the following principles to be implemented and applied as necessary by the County medical society for the guidance of physicians as these programs develop.

1. The county medical society should be satisfied as to the financial and professional integrity of the plan. It should negotiate with the plan sponsors to insure that service charges to the physician are reasonable. It should insist that the plan be open to all physicians on the same terms and that it not exploit or capitalize on physicians' participation in the plan. It should advise the plan that the listing of physicians in directories of participating members is contrary to the ethics of the medical profession.
2. The individual physician may not, because of his participation, increase his fee for medical service rendered the patient. He may not use the plan to solicit patients. He may not encourage patients to use the plan. His position must be that he accepts the plan as a convenience to patients who desire to use it. Plaques or other devices indicating participation in the plan within the physician's office shall be kept to a discreet and dignified minimum. Plaques, signs, or other devices indicating such participation visible outside the physician's office are unacceptable.
3. The use of a bank card in connection with the payment of larger fees—which might normally be paid to the physician in installments—is not to be encouraged. All members of the Association are expected to continue the traditional practice of permitting patients of limited means to pay relatively large fees in installments without interest or carrying charges. Out of respect for the dignity and traditions of the medical profession, the physician may not relieve himself of his obligations "to render service to humanity, reward or financial gain being a subordinate consideration."

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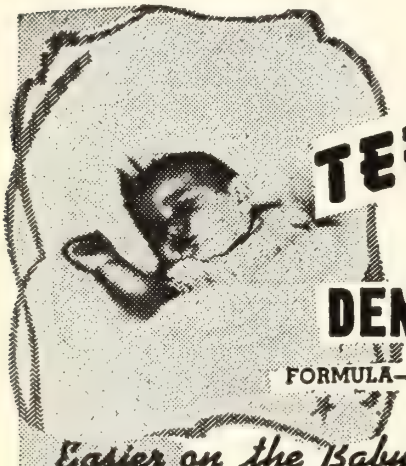

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Home-Centered Health Care

This month we will continue our orientation of programs for the auxiliary:

Growing interest in coordinated home care has developed in recognition of its potential role as that part of a total medical care plan which can best meet the needs of certain patients in certain phases of their illnesses.

There are some basic advantages of home care programs. Experience has demonstrated that:

1. As a rule, the disabled and ill are happier, get well faster, and their dignity is preserved when at home in familiar surroundings.
2. Home care generally is less expensive than hospitalization.
3. In many cases, shortages of hospital beds will become more acute in the years ahead because of medicare and increase in population. Acceptance and expansion of the home care programs obviously would free hospital beds for the acutely or critically ill.
4. It might even eliminate the need for construction of additional hospital facilities in some areas.
5. Coordinated health care might possible prevent health insurance from increasing more because the patients could be dismissed from the hospital earlier.
6. All segments of our population would be able to participate; the young, the middle-aged as well as the elderly, the financially independent as well as the needy.

First we must define what is meant by a coordinated home care program. It is centrally administered and, through coordinated planning, evaluation, and follow-up procedures, provides for physician-directed medical nursing, social and related services to selected patients at home. The physician is the key to the success as it is a medical program under the direction of the physician.

Leadership by the physician in sponsoring, implementing sustaining, and in advisory capacities is essential to assure success. Although the approach will vary with the individual community, experience has shown the most practical approach may be to utilize existing agencies and community resources, for example Visiting Nurse, Home Economists, and voluntary organizations such as American Red Cross and Family Service Agencies (social service workers).

The local medical auxiliary is eminently qualified to provide leadership and direction.

Before inauguration of a program of home centered health care, a reliable appraisal of the community needs should have been assessed.

As prelude to the development of any unit, there should have been established by reliable studies an unquestionable need for the service.

Inevitably, financing of any proposed program must necessarily be an integral part of the original considerations undertaken by the inspired citizens seeking to develop a Home Health Service. In some instances the "seed money" may be tax deductible contributions from the interested professional and public developers. Occasionally foundations, state health agencies, and national health programs may participate. Many programs enjoy support from local United Fund charities. With the success of the program, increasing revenue from fees of the recipients may become significant.

"Home-Centered Health Services" must necessarily vary in different communities. In some meals-on-wheels, telephone companionship for shutins, or friendly visitation; in others, the main value may consist of the more conventional, long established personal services in training the Homemaker—Health Aids.

Woman's Auxiliary A.M.A.
Member Orientation Manual

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Novahistine LP tablets are most useful for relief of nasal congestion in patients without pain or fever.

Novahistine Singlet tablets, which provide analgesic-antipyretic effect, as well as decongestant action, are indicated for upper respiratory infections accompanied by pain, aches and fever.

Whether you prescribe Novahistine LP or Novahistine Singlet, a total daily dose of 3 or 4 tablets will usually provide effective, continuous relief.

Use cautiously in patients with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result.

Each Novahistine LP tablet contains phenylephrine hydrochloride, 25 mg.; and chlorpheniramine maleate, 4 mg.

Each Novahistine Singlet tablet contains phenylephrine hydrochloride, 40 mg.; chlorpheniramine maleate, 8 mg.; and acetaminophen, 500 mg.

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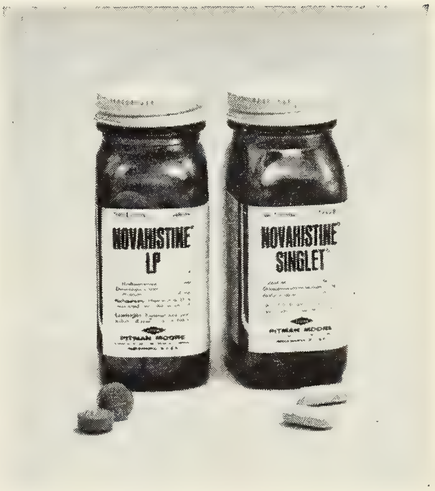


MEETINGS

MEDICINE

March 27 9:30 a.m.-4:30 p.m.

Symposium on Thyroid Function Tests and Diseases

Manchester Memorial Hospital

Speakers: Herbert Selenkow, M.D., Peter Bent Brigham Hospital; David Becker, M.D., New York Hospital; John Brooks, M.D., Peter Bent Brigham Hospital; Bruce Bower, M.D., Hartford Hospital

Program Chairman: Martin Duke, M.D., Department of Medical Education, Manchester Memorial Hospital (643-1141)

Registration Fee $2.00

April 24 9:30 a.m.-4:30 p.m.

Prevention of Cardiovascular Disease—What Is Known and What Is Needed

Mermaid Tavern, Stratford Motor Inn

Speakers: J. Gordon Barrow, M.D., Atlanta, Georgia; Alton Blakeslee, Science Writer

Sponsors: Connecticut Heart Association, Connecticut State Department of Health, Connecticut State Medical Society

Contact: Mrs. Schroeder Burnham, 103 Husted Lane, Greenwich (869-0670 or 756-8113)

Open to all physicians

May 16-18

Cardiovascular Symposium

St. Francis Hospital, Hartford

Speakers: Michael DeBakey, M.D.; Donald Effler, M.D.; C. Walton Lillehei, M.D.; Sidney Blumenthal, M.D.; Benedict Massell, M.D.;William B. Kannel, M.D.; Bernard Lown, M.D.

Contact: Robert M. Jeresaty, M.D., Director, Medical Division, Cardio-Pulmonary Section, St. Francis Hospital

September 9-11

Clinical Electroencephalography

San Francisco

Description: A continuation course designed as a basic review of the applications of the EEG to clinical medical practice.

Sponsor: American EEG Society

Contact: Donald W. Klass, M.D., EEG Course Director, Mayo Clinic

GENERAL

April 10 5 p.m.

Hartford County Medical Association Annual Meeting

Hilton Hotel, Hartford

April 30—May 1, 2

Connecticut State Medical Society 176 Annual Meeting

Hilton Hotel, Hartford

NATIONAL MEETINGS

March

1-3

American Association of Pathologists and Bacteriologists

Drake Hotel, Chicago

13-15

International Symposium on Radiation Therapy

Memorial Sloan-Kettering Cancer Center, New York

15-16

AMA Council on Mental Health

Drake Hotel, Chicago

18-20

American Academy of Pediatrics

Regency Hyatt House, Atlanta

25-29

American College of Allergists

Hilton Hotel, Denver

29-31

American Society of Internal Medicine

Hotel Statler, Boston

CONTINUING MEDICAL EDUCATION

Yale University School of Medicine

Anatomy 201: Special Dissection in Anatomy
Course schedule and fee will be arranged

Anatomy 202: Demonstration in Anatomy
Course runs through May 28; fee $175

Epidemiology and Public Health 100: Introduction to Epidiomology
Designed for general practitioners. Course runs from February 20 to March 14. No fee.

Radiology 304: Clinical Laboratory Application of Radioisotopes
Course runs from February 29 to May 16.
Fee $150.

Institute of Living

Course in Psychiatry for Practicing Physicians
First 10-week course underway since November; second 10-week course begins in April. No fee.

MEDICAL NEWS

Duration Of Antibacterial Therapy

How long should antibacterial therapy be continued? Too brief therapy invites relapse; too prolonged therapy invites toxic reactions, superinfections, and the development or emergence of resistant strains. The recommendations that follow represent a consensus based on published reports, manufacturers' recommendations, and the opinions of Medical Letter consultants.

GENERAL PRINCIPLES — 1. Any infection in which antimicrobial therapy is indicated should generally be treated until evidence of active infection, such as fever and leukocytosis, has been absent for several days. If there is evidence that the infection has been cured, however, a recurrence of fever after several days, or a persistence of fever while the patient is still on antibacterial therapy, should arouse suspicion of reaction to the drug rather than continued or renewed infection. 2. If possible, especially in infections likely to relapse, bacterial smears and cultures should be taken from the site of infection, and should be negative in two or three successive tests. 3. The disadvantages of prolonged therapy (more than two weeks), such as drug toxicity and continued hospitalization, should be weighed against the likelihood of relapse, which is relatively frequent in endocarditis, tuberculosis, brucellosis and osteomyelitis. 4. More prolonged therapy is usually required for premature infants, patients with hypogammaglobulinemia, and those who are receiving immunosuppressive drugs or antimetabolites. 5. When clinically manifested mycotic or bacterial superinfection occurs, the drug may have to be discontinued before completion of therapy, and a new antimicrobial agent active against both the original and the superinfecting organisms substituted. Some superinfections respond merely to cessation of antibacterial therapy and restoration of normal flora.

ACUTE STREPTOCOCCAL PHARYNGITIS AND RHEUMATIC FEVER — In acute pharyngitis caused by Group A beta-hemolytic streptococci, the Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis of the American Heart Association (Circulation, 31:948, 1965) recommends that antimicrobial therapy with penicillin G or alternatives be continued for 1o days. A throat culture two or three days after oral treatment is stopped is desirable, particularly in patients with a history of rheumatic fever or glomerulonephritis. If Group A streptococci are isolated, the course of therapy should be repeated. Other members of the patient's family should have throat cultures taken, and be treated if the cultures are positive.

OTHER ACUTE UPPER RESPIRATORY TRACT INFECTIONS — Most acute upper respiratory tract infections are caused by viruses and do not require the use of antibacterial drugs. When cultures show that H. influenzae, peneumococci, or other bacteria are responsible for severe upper respiratory tract infection, treatment with an appropriate antibacterial agent should be continued for seven to 10 days.

BACTERIAL PNEUMONIAS — Effective treatment of pneumococcal pneumonia can safely be terminated in about seven to 10 days, depending on the absence of purulent complications and the speed of response. Pneumonia due to staphylococci requires more prolonged therapy, however, often extending to three to four weeks after temperature returns to normal. Mycoplasmal pneumonia is usually mild, and mild infection does not require antibacterial treatment.

ENDOCARDITIS — Blood cultures may become negative a few days after treatment is started, but therapy for endocarditis must be maintained long enough to sterilize bacterial vegetation and embolic foci. In bacterial endocarditis caused by organisms highly susceptible to antibiotics, it is usually not necessary to do repeated blood cultures during therapy if the patient gives clinical evidence of response to the drug. After discontinuance of therapy, however, a blood culture is necessary. In endocarditis caused by resistant organisms or when clinical cure is doubtful, a blood culture about once weekly is desirable, with the use of penicillinase-containing media if the patient is receiving penicillin G or V or ampicillin. Streptococcus viridans endocarditis should be treated with penicillin, with or without streptomycin, for four weeks. Staphylococcal endocarditis and endocarditis due to relatively resistant streptococci, such as enterococci, should be treated for at least six weeks.

Reprinted from The Medical Letter on Drugs and Therapeutics, Vol. 9, No. 26, December 29, 1967.

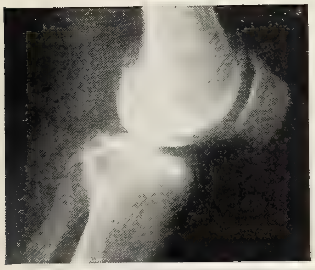
Tandearil®, oxyphenbutazone, 100 mg. tablets

Indications: Osteoarthritis, rheumatoid arthritis, rheumatoid spondylitis, psoriatic arthritis, gout, painful shoulder (peritendinitis, capsulitis, bursitis and acute arthritis of that joint), acute superficial thrombophlebitis, severe forms of a variety of local inflammatory conditions. (In inflammatory conditions not involving prolonged or fatal disease, use only when severity of condition balances potential toxicity.)
The drug has no significant uricosuric action but is of value only in the treatment of acute gouty arthritis.
Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.
Warning: Tandearil is an analog of phenylbutazone; sensitive patients may be cross-reactive. If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.
Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make regular blood counts. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.
Adverse Reactions: The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by with-

“Pain Break” for an osteoarthritic.

Tandearil can ease it.

At 46, her knees still look good on the outside. But inside, there may be the familiar picture of osteoarthritis.



If aspirin doesn't help, Tandearil often will. Pain and stiffness begin to ease up in 3 or 4 days. You can often maintain response with a daily dose of only 1 or 2 tablets.

Of course, Tandearil is not for every osteoarthritic. Select your patients carefully and follow them in line with the Contraindications, Precautions, Warning, and Adverse Reactions listed below.

But for many aspirin-stubborn osteoarthritics, let Tandearil ease the unwelcome pain breaks of osteoarthritis.

Tandearil®
oxyphenbutazone

holding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis or a generalized allergic reaction similar to a serum sickness syndrome may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Osteoarthritis: Initial: 3 to 6 tablets daily in divided doses. It is usually unnecessary to exceed 4 tablets daily. A trial period of 1 week is adequate to determine response; in the absence of a favorable response, discontinue. Maintenance: An effective level is often achieved with 1 or 2 tablets daily, do not exceed 4 daily. 6562-VI(B)R2

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NEW BOOKS IN REVIEW

TOUCH, HEAT AND PAIN, Ciba Foundation Symposium by A. V. S. de Reuck, M.Sc., D.I.C., A.R.C.S., and Julie Knight, B.A., Little, Brown and Company, 1966. 124 illustrations, 389 pages. $14.00.

Reviewed by: LOUIS H. NAHUM

The purpose of the Ciba Foundation is to promote international cooperation in medical and chemical research. Its domicile is in London where world scientists convene to participate and are housed in their home Portland Place in London.

In this symposium twenty-five specialists in the field of anatomy, cell biology, neurology, pharmacology, physiology, psychophysics and zoology have combined to give us a valuable medical and chemical look at the macromolecular complexes within a membrane and show the relationship between the nerve cells of the periphery and the central nervous system.

There are five sections. One is on discrimination of quantitative differences in stimuli in man. One is on the structure of the receptor organ where we find that there is no naked axoplasmic filament which is pretty well encased in a neurilemma extending out from the neurone. A third section is on basic mechanisms, biophysics of supporting tissues and receptors. A fourth on relation of single receptor activity to parameters of stimuli. A fifth is on the relation of activity of population of receptors to parameters of stimuli.

The lively discussion after each paper is highly technical and will appeal to basic scientists working in the field.

CARDIOVASCULAR SURGERY 1966. Edited by C. Frederick Kittle, M.D. American Heart Association, Monograph, Number Sixteen, 1967. 243 pp. $3.00

Reviewed by: WILLIAM W. L. GLENN

This Monograph #16, published by the American Heart Association and distributed as a Supplement of Circulation, is the fourth annual publication of selected surgical presentations at the 39th annual meeting of the American Heart Association. The Monograph is comprised of 34 papers.

Eleven papers were devoted to operations on the cardiac valves. Two of the papers recounted early experiences with homotransplants. The nine other papers were concerned with problems related to prosthetic replacement of the cardiac valves.

A collected series of patients undergoing embolectomy for massive pulmonary embolism was reported.

The problem of procuring a healthy heart for transplantation, when other obstacles to this procedure have been hurdled, was discussed.

Six papers were concerned with congenital heart defects. The following subjects were presented: the management of infants with total anomalous pulmonary venous drainage requiring operative correction using hypothermic arrest of the circulation; correction of Ebstein's anomaly by prosthetic valve replacement of the tricuspid valve; technical problems encountered during total repair of the tetralogy of Fallot patients with a splenic artery-pulmonary artery shunt; operative procedures performed for cardiac defects associated with corrected transposition of the great vessels was reported; results of closure of atrial septal defects in patients over the age of 45, and a new technique for banding the pulmonary artery to allow restoration of the normal sized lumen when the band is removed.

Three articles were presented on myocardial revascularization. One of these explored the concept that a demand for oxygen was needed before collateral channels between the internal mammary implanted in the heart, and the myocardium will develop. A second study reviewed the coronary angiograms in 315 patients with angina pectoris. The initial applications of gas endarterectomy to patients with occlusive coronary artery disease was described in the third article.

Peripheral vascular problems were covered in three articles. The cause of hyperemia and edema of the leg occurring after a revascularization procedure was investigated. The results of thromboemdarterectomy, synthetic bypass grafting and autogenous saphenous bypass grafting were compared. Also reported was the treatment of acute dissection of the aortic wall (dissecting aneurysms) by the administration of hypotensive drugs.

Seven papers were presented on problems related to partial or total cardiopulmonary bypass. Three of these were concerned with changes in the lungs during and after total bypass for cardiotomy. Another article discussed the relative evaluation of left heart bypass with counterpulsation as techniques for myocardial augmentation. In another study the influence of oxygen flow rate of arterial oxygenation and acid-base balance during cardiopulmonary bypass with the use of a disc oxygenator was described.

The last two papers in the Monograph concerned a study which was made to determine the extent of damage to the RBC during and following prolonged pumping in the canine, and myocardial function following electrically induced ventricular fibrillation, also in the canine.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Atlas of Roentgenographic Positions. Volume one of three volumes, third edition. Edited by Vinita Merrill. The C. V. Mosby Company, Saint Louis, 1967. 309 pp.

Atlas of Roentgenographic Positions. Volume two of three volumes, third edition. Edited by Vinita Merrill. The C. V. Mosby Company, Saint Louis, 1967. 526 pp.

Atlas of Roentgenographic Positions. Volume three of three volumes, third edition. Edited by Vinita Merrill. The C. V. Mosby Company, Saint Louis, 1967. 878 pp. $46.50.

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176th Annual Meeting
Connecticut State Medical Society
Hartford Hilton Hotel, Hartford

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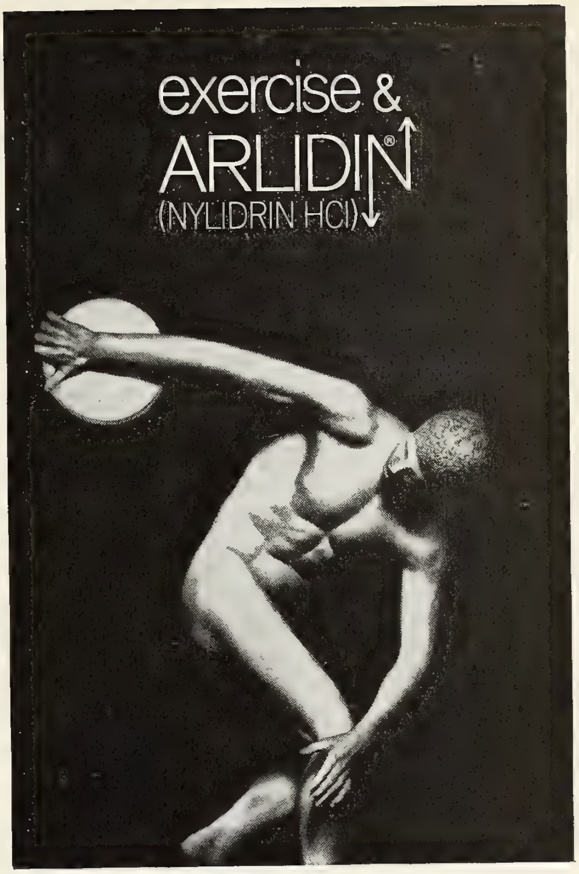

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Connecticut Medicine

MANUSCRIPTS

Manuscripts, including references or bibliography, must be typewritten, double-spaced on white paper 8½ x 11 inches with adequate margins on firm paper. The original copy, not the carbon copy should be submitted. Carbon copies or single spaced manuscripts will not be considered. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Receipt of manuscripts will be acknowledged and unused manuscripts returned. *Accepted* manuscripts become the permanent property of the JOURNAL and may not be reprinted elsewhere without permission from both the author and CONNECTICUT MEDICINE. The author is responsible for all statements made in his work, including changes made by the copy editor.

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The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the JOURNAL (listing name and initials of author, title of article, journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

ILLUSTRATIONS

Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. CONNECTICUT MEDICINE will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

NEWS

Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

ADVERTISING

All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by CONNECTICUT MEDICINE.

Material other than original articles should be received not later than the 10th of the month PRECEDING date of issue.

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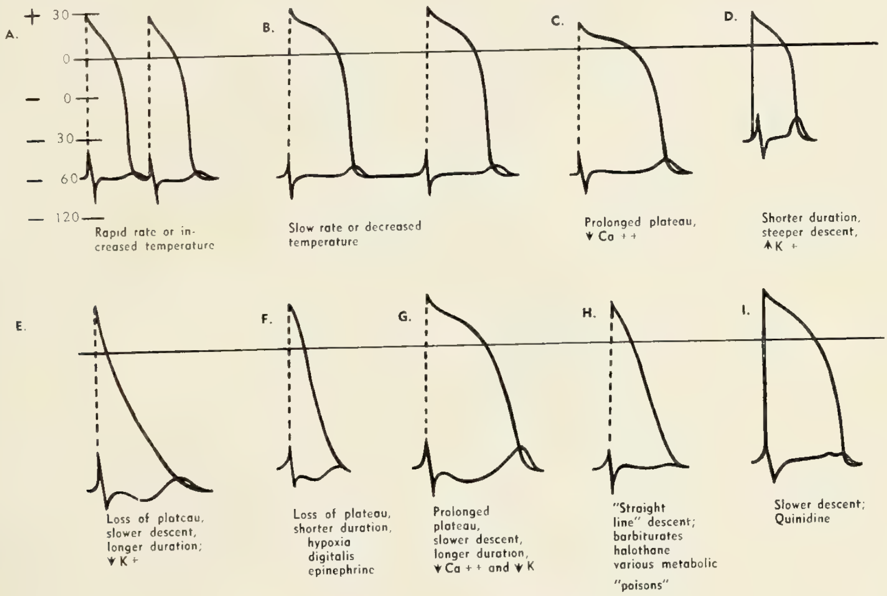

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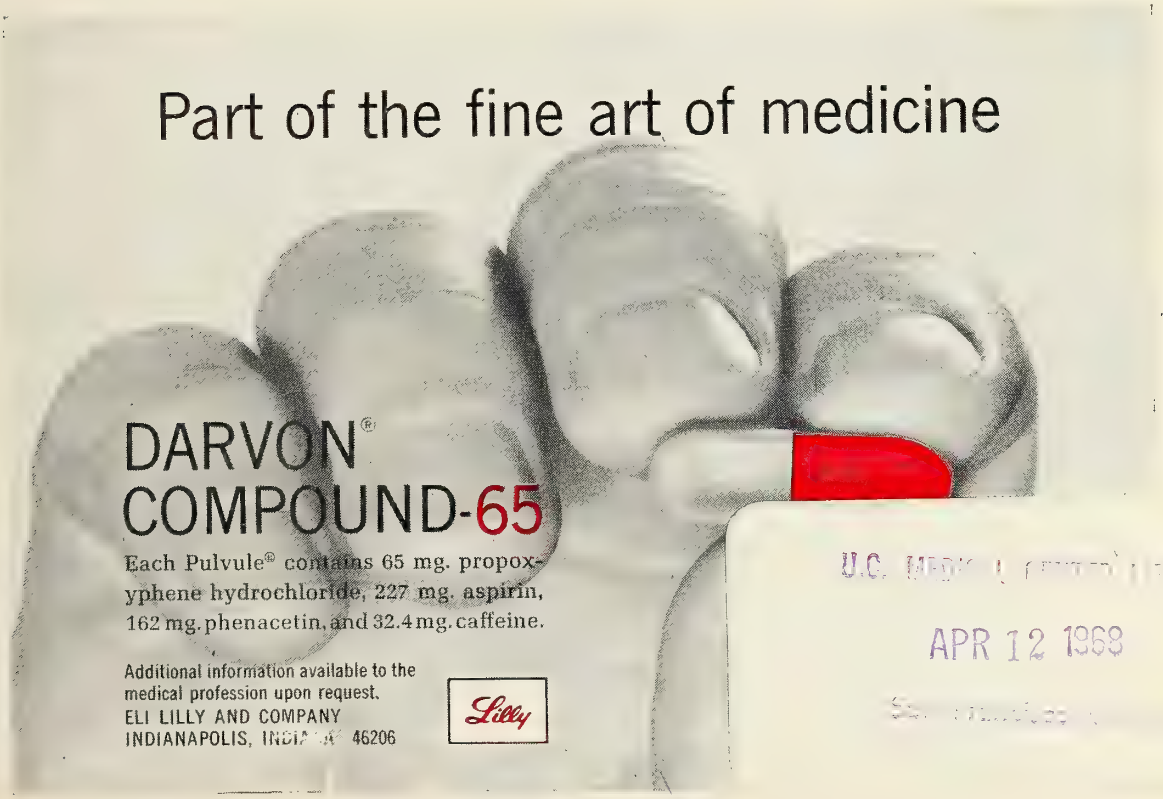
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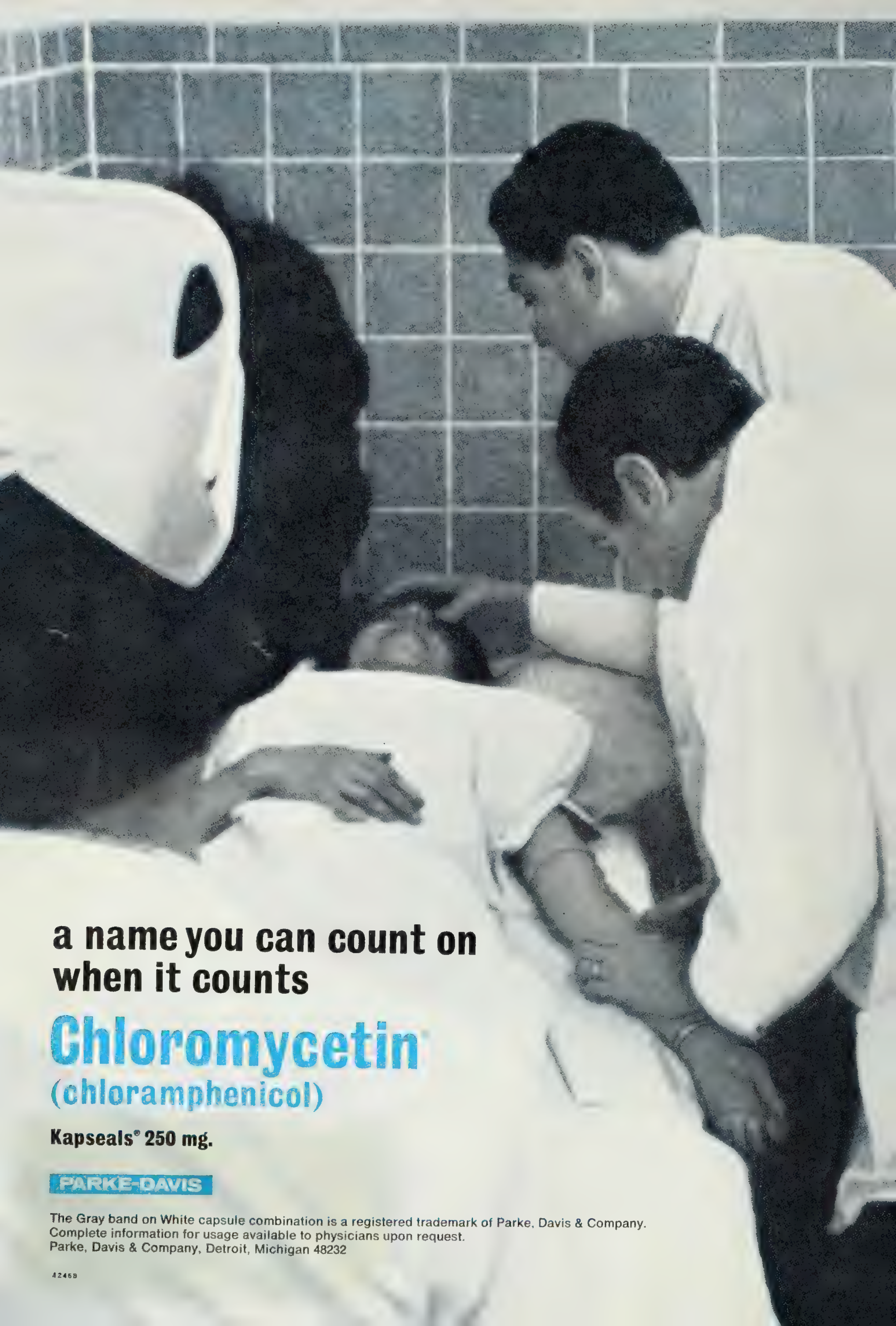

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Connecticut Medicine

editorials

Heart Transplantation: Treatment Or Experiment

Is the heart transplantation operation in human's now in the stage of treatment of a sick person or is it an experiment. Dr. Christiaan Barnard regards his heart transplant operation on Washkansky "a form of treatment of a sick person". There are serious reasons to question the validity of this assertion. Several kinds of problems must be solved before transplantation surgery may be regarded as treatment rather than experiment. One is the matter of surgical technique. One is the problem of overcoming the genetic barrier to transplantation. One is to overcome the physiological disturbances resulting from implanting a denervated heart which has also severed its lymphatic drainage system.

The matter of surgical technique is the easiest of the three problems to overcome. Given thorough preparation in animal surgery and the development of mechanical aids and supportive procedures, success is attainable and is largely dependent on the skill, daring and general medical sophistication of the surgeon and his team. The jump from performing the operation in animals, to doing it in man is not too large and the probability of surgical success can be estimated with reasonable certainty in advance. The actual performance of the Washkansky operation did indicate that Barnard's group and similar groups in this country had reached the point in experience, skill, daring and sophistication to carry it out with technical success.

The second problem that of overcoming the genetic barrier to transplantation is a more critical one. It is hardly likely particularly in the case of heart transplantation that complete donor-recipient compatibility will be available in any particular case. While some organs may be more susceptible to rejection than others, all are subject to the action of histo-compatibility factors. In the case of the heart nothing is known about the relative susceptibility of the nervous and conduction system and this is a special problem. For the time being reliance must be placed on the use of immunosuppressive drugs and radiation. These create difficult problems for the patient who already is in a debilitated state. Dr. Barnard has stated that perhaps the heart will require less immunosuppression than for example a skin transplant would, but they don't know.

There are, however, ways of minimizing the histocompatibility barrier. Matching of red cell types is elementary. Matching with respect to transplantation antigen is more pertinent to this discussion. This is most conveniently accomplished by the detection of individual leucocyte antigens with suitable isoimmune antiserums (leucocyte typing) or by the use of matching tests such as mixed leucocyte culture typing (MLC typing). The results of both of these kinds of tests are at least partially predictive of transplantation success.

Evidence is accumulating that there is a single major histocompatibility genetic locus in man and that either of these types of tests can detect genotype agreement for this locus.[1] There is an excellent prospct that minor incompatibilities may be suppressed without heroic efforts, provided donor-recipient compatibility for the major locus is assured.[2] An approach to this objective should not be impossible even when donors are rare as in the case of a heart transplant.

THE COVER

Figure 1. Diagrammatic presentation of the relation between the ventricular transmembrane action potential and the electrocardiogram. A-1. Effect of various factors which alter the duration and velocity of the repolarizations. (See text.) The scale on the top left represents amplitude in millivolts. The upstroke of the action potential is represented by an interrupted line except in D. and 1. where the upstroke is drawn as a solid line to indicate the decreased velocity of depolarization accompanied by hyperpotassemia and quinidine. The short horizontal lines transecting the upstroke of the aciton potential represent the level of O mV.

The importance of these considerations are great enough to justify the delays that the performance of the tests would impose, particularly since many possibilities exist for the maintenance of recipient and donor through the period in question. The importance of the sex problem cannot be evaluated. Apparently rbc typing was performed in advance of the Washkansky operation. Apparently also limited leucocyte typing was performed but not until after the operation had been initiated. One may infer from press reports that MLC typing or other matching tests were not performed. No prior attempt was made to match donor and recipient with respect to transplantation antigens. There is every indication from available information that they were actually incompatible as most unrelated donor-recipient combinations would be when chosen at random. Under these circumstances massive immunosuppression and radiation were adjudged to be required and were applied. It is not surprising therefore that the patient died of pneumonia. Clearly the histocompatibility problem was not dealt with in the Washkansky case even within available limits.

The histocompatibility problem will in time be solved but how can the physiological problem be solved. Assuming that the conduction system will be spared destruction by rejection, the nervous control of the heart will not regenerate. The heart will be left operating without signals from other organs via the central nervous system. It will not know when to beat fast and when to beat slow, when to beat forcefully and when to beat normally. Some of this information the physician might be able to supply by drugs but the minute to minute regulation of the heart in the interest of patients needs will be absent.

The effect of severing the lymphatic drainage of the heart has not even been considered. Unless the protein in the interstitial fluid of the heart is carried away by the lymphatics exchange between plasma and interstitial fluid would cease and cells would be chocked off from receiving nutriments and excreting waste products. It is valuable that the quantity of interstitial fluid be maintained at a minimum by the lymphatic channels so that transfer of these substances can occur. Many diseases are being recognized in which obstructed lymph return in the heart has led to inefficient contraction or even cellular death.[3]

The way the heart is transplanted, the atria around the great veins are retained and the donor heart is sewed to the cut edge of the atria. The pulmonary artery and aorta are then anastomosed. The donor heart is then cut off from nervous connections and probably the lymphatic vessels obliterated in the suturing. Even if some remain open, the lymph can go nowhere except in the pericardium or mediastinum. How well the recipient vestigial atria remain nourished is not clear.

It is clear that the operation should not be justified as treatment with all the unknown variables. If it was an experiment it must be adjudged as premature. The argument is offered that the operation succeeds in some dogs. But heart transplants in dogs succeed or fail for reasons that are completely unknown. One would suppose that histocompatibility and the problem of immunosuppressors should be clarified by animal experiments before human surgery be attempted. Furthermore ways should be found for recreating nervous connections to the heart and lymphatic channel anastomoses to restore the transplanted heart to more nearly physiological condition.

Since the Washkansky case there have been several other unsuccessful transplants all receiving their measure of publicity which was so great as to generate irrestible pressures for additional attempts. Perhaps there should be a frank and open discussion of the problems raised above within the scientific community before further attempts are continued. Obviously surgical, biological and physiological problems are involved and perhaps problems of medical ethics and public information. Perhaps it is time that a series of guidelines be developed which could be applied to future human organ transplantation.

L.H.N.

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answer that the tobacco industry offers to the devastating figures that Surgeon General Stewart released pointing out that 275,000 people in this country die annually that would not die if they did not smoke? The answer seems to be "it's all statistical nothing is proved experimentally!"

Okay, well let's see what it is that the cigarette smoker inhales. Most people when they consider air pollution think of the automobile, the smokestack or the trash burners. It's time then to point to a most damaging source of air pollution, the cigarette. One of the toxic products of the automobile exhaust is carbon monoxide (CO). Exposure for one hour to a concentration of this gas of 120 parts per million causes inactivation of about 5 per cent of the body hemoglobin by forming CO hemoglobin. Concentrations of CO as high as 100 ppm. often occur in garages, in tunnels, and behind automobiles. Such concentrations are tiny in comparison with those (42,000 ppm.) found in cigarette smoke!

The smoker survives because most of the time he breathes air not so heavily polluted. Nevertheless the smoker can carry 15 to 20 per cent CO hemoglobin for hours and seriously reduce the oxygen supply to already compromised areas in the brain, heart and elswhere whose arteries are narrowed by atherosclerotic disease. Furthermore, in a poorly ventilated smoke-filled room concentrations of CO can easily reach several hundred parts per million thus exposing smokers and non-smokers present to a toxic hazard The headache and fatigue that those exposed experience after a time in such an atmosphere is no accident and not psychosomatic.

Another air pollutant issuing from automobiles is nitrogen dioxide (NO_2). This gas is acutely irritating. It also gives rise to nitrite which is a potential mutagenic agent. Concentrations of NO_2 as high as 3 ppm. have been noted in Los Angeles and levels of 5 ppm are considered dangerous. Cigarette smoke contains 250 parts of NO_2 per million.

Many of the toxic agents in cigarette smoke do not have counterparts in ordinary air pollution. One of these, hydrogen cyanide, is particularly noteworthy. It is highly active against respiratory enzymes. Long term exposure levels above 10 ppm. are dangerous. The concentration of CN. in cigarette smoke is 1600 ppm. Another inorganic pollutant that has been found in cigarette smoke is polonium 210. This is a radioactive substance taken up by mucus membrane in the bronchial tree where it is permanently trapped and could by its radiation lead to malignant degeneration.

These inorganic pollutants are four of many noxious substances that have been found in cigarette smoke. Among others are acrolein, aldehydes, penols and carcinogens an important one of which is benzo(a)pyrene. Evidence points to synergistic effects among toxic agents. The phenols though not themselves notably carcinogenic increase markedly the carcinogenic potency of benzo(a)pyrene. Add these carcinogenic effects to the radiation of polonium 210 and we can begin to appreciate why lung cancer in smokers is so high.

The toxic effects of cigarette smoke are also enhanced by other environmental factors. A recent study of asbestos workers showed a very high incidence of lung cancer among smokers in contrast to a low incidence among non-smokers. In a group of 283 asbestos workers who had a history of cigarette smoking, 24 of 78 deaths were due to bronchogenic carcinoma. Of 87 asbestos workers who were non-smokers none died of lung cancer during a comparable period. A similar study of uranium miners stricken with lung cancer has revealed a similar effect related to smoking. The rate of fatalities was much higher among smokers than nonsmokers.

Another example of a synergistic effect is seen in the smokers who breathe polluted urban air. The incidence of lung cancer is higher in the city than in rural areas.

The smokers pay for their habit with chronic disease and shortened life. Involved are the individuals decision and his very life. One might therefore think that since the principal effects of smoking are borne by the smokers themselves, that a person who wishes so to destroy himself should have this "right." The sad fact is that he has a wife, children, friends who will also suffer. Society is involved since when the smoker becomes disabled 8 or 16 years before his time he becomes a burden on his family and society. By his drive to self destruction he infringes upon the rights of others in yet another way. When the individual smokes in poorly ventilated spaces in the presence of others, he becomes a serious contributor to air pollution and infringes upon the rights of others present who have a right to an uncontaminated environment.

L.H.N.

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Heart Rate And Cardiac Output In Atrio-Ventricular Block

The efficiency of artificial pacemakers in the treatment of Adams-Stokes attacks is clearly established. This point is well illustrated if one compares the experience with a group of patients with complete heart block who received permanent pacing by an artificial pacemaker and others who did not. Sowton[1] reports 544 patients with complete A.V. block who were paced with an implanted pacer. Eighty-three per cent lived for a year or more as compared with 60 per cent in a group of 119 similar patients treated conservatively.[2] Of course, pacemakers have their own problems such as wire breakage, battery failure and in the case of transvenous pacing an undesirable focus for initiating the ventricular contraction and even the possibility of ventricular wall perforation. Nevertheless, there is no doubt that pacemakers have improved the prognosis in cases of complete heart block.

There is another indication for the use of the pacemaker, that is the existence of refractory heart failure in association with a slow ventricular rate in complete heart block. In the presence of extensive myocardial disease the cardiac output is known to decline as the heart rate falls below 60. Both Escher[3] and Bevegord[4] have demonstrated a progressive improvement in the cardiac output as the ventricular rate is increased from 30 to 60 beats per minute. It is not so clear-cut as to what happens to the cardiac output when the heart rate is within the physiologic rate (60—120 per min.). Some have reported no change in cardiac output in patients with complete block if the rate was increased from 60—120 beats per minute.[5,6] Other observers have noted a steady increase in the cardiac output as the rate increased from 39—100.[7]

These conflicting results are probably due to the type of patient studied. Some patients with complete block also suffer from extensive myocardial disease whereas others have little or no evidence of myocardial disease. In the group without myocardial disease (Sowton[8]) the cardiac output seems not to depend on heart rate. By contrast in the patient with extensive myocardial disease the cardiac output is rate dependent and increases as the heart rate increases. It is not difficult to interpret this finding if we recall that a heart with extensive myocardial disease and a very slow rate means over distention of myocardial fibers which are now operating on the descending slope of the Starling curve. This can only contribute to the heart failure.

On the other hand shortening the diastolic period by producing a more rapid heart rate, reduces the filling time of the ventricle and, therefore, the end diastolic volume and pressure. The over distention is relieved and a more efficient contraction follows.

The ability to improve the cardiac output by increasing a slow heart rate to physiologic levels has been utilized by a number of investigators in the treatment of congestive heart failure. Thus Miller and Bellet[10] reported the result of their studies on two patients with severe intractable congestive heart failure in association with complete heart block. One patient with a paced rate in the physiological range lost 31 lbs. of edema fluid over a period of 20 days. The second showed marked improvement in exercise tolerance although the decrease in weight was not as remarkable. The mechanism by which the edema fluid is mobilized is probably improvement in the heart contractility which permits increased cardiac output and increased delivery of sodium to the kidney for excretion.

This was well shown by Friedberg and his associates[11] who reported their results on four patients with complete heart block, first with idioventricular rate of 30–40 beats per minute at which time the glomerular filtration rate was markedly reduced. As the heart rate was increased, the glomerular filtration rate improved and their ability to excrete sodium also increased.

Another question that arises is whether muscular exercise has any effect upon the cardiac output in cases with complete heart block. Recent evidence indicates that in the absence of extensive myocardial disease and congestive heart failure exercise at any fixed heart rate will increase the stroke volume.[12] We know that there is increased venous return in exercise because of peripheral dilatation induced by muscular contraction. In consequence there will be increased ventricular filling and increased stroke volume. Besides this factor the response is also effected by increased beta adrenergic drive to the myocardium which also enhances myocardial contractility. Finally we must remember that the peripheral dilatation induced by exercise decreases the aortic diastolic pressure and facilitates emptying of the left ventricle.

The final point to remember is that not every case will yield the desired result of improving the cardiac output by increasing the rate. The hemodynamic response to pacing may be altered by intensive diuresis that may result in patients with congestive heart failure and heart block. The re-

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duction in blood volume following diuresis may diminish cardiac filling pressure to such an extent as to reduce cardiac output even though the patients improve symptomatically.[13]

L.H.N.

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Diphenylhydantoin In Cardiac Arrhythmias

Ever since Merritt and Putnam[1] introduced diphenylhydantoin (DPH) for treating convulsive disorders, effects on the heart were also noted. It was reasoned that the arrhythmias after coronary occlusion might arise from a mechanism similar to that of focal cerebral impulses that produce seizures. In a valuable series of experiments, Harris and Kokernet[2] demonstrated that adequate amounts of DPH controlled ventricular tachycardia in dogs after ligation of the anterior descending coronary artery. Since them reports began to appear on the use of DPH in experimental arrhythmias induced by digitalis intoxication, epinephrin injections in combination with cycloproprane anesthesia, electrical stimulators and focal application of aconite. The arrhythmias induced in these studies were both atrial and ventricular.

In 1958, Leonard reported a case of a 42 year old man with ventricular tachycardia associated with myocardial infarction. Intravenous DPH controlled the arrhythmia which had been refractory to high doses of procainamide. In 1964, Osborne[3] reported that DPH was effective in treating ventricular arrhythmias associated with cardiac surgery, cardiac catheterization and some supra-ventricular arrhythmias due to digitalis toxicity. Many further reports have since appeared. The most recent report is that by Mercer[4] on the use of DPH in 774 arrhythmic episodes including 33 in whom hazardous arrhythmias occurred during induction of general anesthesia. Of theoretical interest is the success of DPH in preventing episodic multifocal ventricular premature beats because it suggests that the drug acts to antagonize the sympathetic mechanisms that have been shown to operate in the production of ventricular arrhythmias.[5]

DPH was in Mercer's studies administered intravenously over a period of 2—5 minutes, the initial dose was 125 mg. Then if no effect was achieved a second dose was given in 15 minutes. The largest dose given over several hours was 1 gram. It is significant that Mercer found no adverse effect upon subsequent use of other drugs by prior treatment with DPH. It is also interesting that there was no response to DPH in cases of atrial flutter and fibrillation.

The best effect was when factors precipitating the arrhythmia were of short duration such as during induction of anesthesia, after cardioversion and cardiac surgery. Intravenous DPH proved extremely valuable, highly efficacious and rapid acting as well as safe after operation and angiography. Some patients with persistent ventricular irritability responded well to DPH by intravenous drip with a total 24 hour dose of 1 gram or less. The response to digitalis intoxication was excellent and in arteriosclerotic heart disease and acute myocardial infarction it was excellent in one quarter and partial in one-third of the cases. Of further value to those who will use this drug clinically is the fact that complications were very few in this large series. Mild nausea, a headache for 1—2 minutes, only a

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Warning: May be habit-forming.

Precautions: Tuinal should be used cautiously in patients with decreased liver function, since prolongation of effect may occur.

Adverse Reactions: Idiosyncrasy, such as excitement, hangover, or pain, may appear. Hypersensitivity reactions occur in some patients, especially in those with asthma, urticaria, or angioneurotic edema.

Overdosage: C.N.S. depression. Symptoms—Depression of respiration and of superficial and deep reflexes, slight constriction of the pupils (in severe poisoning, dilation), decreased urine formation, lowered body temperature, coma. Treatment—Symptomatic and supportive (gastric lavage; intravenous fluids; maintenance of blood pressure, body temperature, and adequate respiration). Dialysis may speed removal of barbiturates from body fluids.

Dosage: 50-200 mg. (¾-3 grains) at bedtime.

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mild fall in arterial pressure were all that were encountered. Thus the drug is relatively safe, its effect transient and the electrophysiologic effects make it attractive in digitalis intoxication.

Of course, the drug is often given to seriously ill patients who also have such complications as hypoventilation, acidosis and serious impairment of cardiac function which should be corrected. In such instances monitoring the patients rhythm is necessary and resuscitative and defibrillatory facilities should be at hand or on call. We need also to remember that the drug is congugated in the liver and when liver function is impaired greater caution is required.

For temporary maintenance therapy after acute treatment of an arrhythmia with DPH many have found 100 mg. orally or I.M. every 6–8 hours generally adequate. For long term prevention of recurrent arrhythmias in adults oral administration of 200–400 mg. of DPH in divided doses seems highly efficacious in regular tachycardias of both supra-ventricular and ventricular origin.

Helfant's[6] studies throw some additional light on the differences of action of DPH and procainamide and quinidine which are also used as anti-arrhythmic agents. DPH antagonizes the action of digitalis on the a-v node by decreasing the block caused by the glycoside. It also reduces excitability and automatism as do procainamide and quinidine but unlike these drugs it does not increase the effective refractory period and unlike them DPH also has no influence on atrial flutter and fibrillation. Procaine prolongs i.v. conduction especially accentuated in the digitalis poisoned heart and, therefore, the chances of procainamide potentiating a re-entry type of arrhythmia is greater than with DPH.

It would appear from Mercer's studies and Helfant's[7] that DPH could become the drug of choice in abolishing or preventing cardiac arrhythmias other than atrial flutter and fibrillation.

L.H.N.

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The Right To Privacy

We are beginning to recognize several new "rights" of our patients. One is the right to privacy. Another the right to have pain. A third is the right to truth from his doctor. A fourth is a right to die and not to have his misery prolonged with a hopeless disease. The right to privacy is both an ethical and legal formulation. Now that human experimentation is on the march, the invasion of one's privacy is more than a theoretical problem. Furthermore, with new technological devices that can "invade privacy," the problem has been extended far beyond the medical sphere and has been the subject of much current publicity, both in government and in human experimentation.

At about the time the government was investigating the danger of data banks to privacy a research project involving the injection of live cancer cells into elderly terminal patients without their knowledge or consent received much news coverage and criticism. All this has created a climate in which researchers working in sensitive areas might become uncertain and anxious. The famous statement attributed to Hippocrates may be appropriate here. "Life is short and the art long; the occasion instant, decision difficult, experiment perilous." We are not told whether Hippocrates meant that experimentation is perilous for the subject, the experimentor or both. However, the experimenters need not feel anxious if it is called to their attention that no investigator has run into serious legal difficulty, if he has competently conducted his research and observed the basic ethical principles of investigation. What are these ethical principles?

The most generally recognized ethical guidelines are those outlined in the "Nuremberg Code" and the more recent "Helsinkie Code" promulgated by the World Health Organization. It is remarkable, however, that nowhere in these codes is a discussion of the subject's right of privacy even though this is an important aspect of the proper conduct of an experiment. How do we define this "privacy?" The following definition as offered by Ruebhausen and

Brinn[1] is quite adequate for our purpose: "The essence of privacy is no more and certainly no less than the freedom of the individual to pick and choose for himself the time and circumstances under which, and most importantly, the extent to which his attitudes, beliefs, behavior and opinions are to be shared with or withheld from others." Investigators informing their subjects, regarding information obtained, has varied greatly from completely surreptitious observation to completely open cooperative endeavors.

The right of privacy includes both obtaining the subject's permission before the research and also his permission to disclose the information obtained from the resulting research. Adequate safeguards for privacy, therefore, requires that the investigator may not eavesdrop or surreptitiously obtain sensitive information linked to a particular patient. Once a person has decided to disclose some information about himself, the investigator remains under some ethical obligation to see to it that the information is not subsequently used in a manner that harms the subject. The patient must be protected from future misuse of the information especially if it remains linked to the subject in such a way that he is identifiable by it. Such information must be treated as confidential and not available to associates, police and especially clerical personnel whose tongues may be long.

Schwitzgebel[2] points out that information acquired during research, unlike similar information acquired during therapy, does not have a privileged status under law in many states. Clearly consideration should be given to enactment of statutes that would grant such a privilege.

How can we help to preserve the subject's rights through anonymity after voluntary participation? One way is to assign a number to a subject and then a "key" could link names and number which should then be held by a reasonable, independent person. The key should then be used only with the consent or when a court has ordered its use as evidence. If group data rather than individual data are needed, then questions could be presented on separate unidentifiable forms so that it would be difficult to match a subject's answer on one item with his answer on another.

Much of the concern about the invasion of privacy has arisen from the rapid development of technologic devices capable of obtaining and storing information about individuals. We note that numerous government agencies are collecting private information about most of us and that a national data center is being proposed to pull together the scattered statistics in government files on citizens and provide instant and total recall and exposure. The names of most Americans appear repeatedly on government files, social security records, police records, medical and psychiatric records, court actions, security reports and others including personnel and job files—for a total of 2.8 billion listings. The Defense Department has 14 million life histories in its security dossiers, the Civil Service 8 million and countless others. These government agencies have 100 million punch cards and 30,000 computer tapes containing information about people and companies. Agencies would show information with one another and scholars, businesses and state and local officials would also have access.[3]

Professor Westin[4] says that "the trend towards greatly increased collection of personal data, exchange of information among the collectors and consolidation of such personal information into central data banks represents by far the most serious threat to privacy in the coming decade." "The file are not equipped to correct errors, allow for extenuating circumstances for redemption is likely to be incomprehensible to a computer. Mr. Vance Packard says, "Americans increasingly and rightly resent their being numbers, controlled by a computer and the accelerating depersonalization of individuals." Representative Gallagher made another point recently before Congress. "In order to create more benefits governments think they need to know more about their people. The more government knows the less the individual has left of himself which is his own." . . . .

Safeguards are needed which cannot be left to people's good intentions. Professor Hamblin[5] suggests that subjects could fill out special answer sheets without their names on them that could be immediately read by an optical scanner and fed directly into a computer. The subject could then destroy his answer sheet. The information on a series of patients would be given to the investigator in summary form. By this on-line testing anonymity could be preserved without the investigator meeting the subjects. A computer could store the information that would require a series of "keys" to be retrieved. Also, information given in response to a particular question could be dated and automatically erased after a terminal date. A computer could be programmed to reject "improper" questions about the individuals and give out only group data. A record could also be kept in the computer of anyone requesting information and the questions asked.

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Finally, a committee of professional persons familiar with a research could be set up as suggested by the Surgeon General to look after subject welfare and see that adequate safeguards were maintained. It might also be possible to involve some of the subjects in overseeing the use of information obtained from them. Possession of disallowed information should also carry some penalty.

The use of such measures and perhaps others might help to protect a subject's privacy and reduce present and future hazards resulting from participation in human experimentation.

L.H.N.

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Experiments in Medical Education—Yale's New Medical Curriculum

The Winternitz idea of making the Yale Medical School into an experimental school in medical education is finally about to be realized. It was with this idea that he induced the then Rockefeller Institute to build the Institute of Human Relations. It was this idea that led to bringing patients into the physiology classes in the first year by Hebbel E. Hoff and this writer for many years. At that time it was intended to bring meaning into abstract physiologic principles by showing the results of their derangement in the sick person. Thus at that time the sick person was used to arouse the student's interest right from the start into the clinical meaning of abstract knowledge. In the new Yale curriculum the student will be exposed to clinical medicine early and abstract knowledge will be brought to the embryo physician to illuminate and enrich his understanding of the sick person.

The new curriculum calls for earlier introduction of clinical experience while retaining time allotted for preclinical courses. The first half of the first year is assigned to teaching "basic sciences." This includes the basic, behavioral, social, epidemiologic and preclinical sciences. During the second semester of the first year significant portions of the courses Introduction to Clinical Medicine, Laboratory Medicine, Pathology and Pharmacology will be completed. The remainder of courses will be given in the beginning of the second year.

The inclusion of significant portions of the courses, Introduction to Clinical Medicine, Laboratory Medicine, Pathology and Pharmacology, in the first year will prepare the student for clinical activity during the first summer. Each student will be required to have six weeks of clinical experience during one of the two six week periods available during the first summer. By putting students at the bedside this early in their careers, the hope is to encourage a sense of compassion that a doctor needs. Dr. Redlich, the dean states "if the student spends his first two years in the classroom studying cells and molecules as is now the case he sometimes loses the wonderful idealism that made him want to be a doctor in the first place." It is to be hoped that this reorientation of the curriculum can accomplish this purpose although some think that bringing the student to the patient very early may merely set in motion earlier the feelings about sickness and suffering which the student now begins to experience in the third and fourth year.[1]

The sixth, seventh and eighth semesters will be devoted to specialized programs or "tracks." Each track will contain the following curricular activities:

(a) a series of graduate level science courses relevant to the student's goals. The courses will be concentrated in the sixth semester with a progressive decrease in the seventh and eighth semesters.

(b) one or more courses which correlate clinical medicine and fundamental science.

(c) appropriate clinical experience starting in the sixth and progressively increasing throughout the seventh and eighth semesters.

(d) out-patient clinic experience (medicine and pediatrics) at least two half-days per week for one eighteen-week semester, or one half-day per week for two eighteen week semesters.

The research thesis will continue to be a requirement for graduation. Time for thesis work will be available during the first, second and third summers as well as during the three track semesters. The student may elect to take Part I of the National Board examination at the end of the second year or at the end of the third year. In either case he may take it either in June or in September. He will

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continue to take Part II of the examination at the end of his eighth semester.

The principle advantages of the plan seem to be the following:

1. Adequate time is provided for the teaching of required fundamental science courses at the beginning of the curriculum.
2. The goal of earlier clinical experience is achieved by providing six weeks of this in the first summer.
3. Three full semesters are provided at the end of the curriculum for specialized programs. This will allow the student to plan with his advisor, a major portion of his curriculum according to his own talents and interest.
4. The teaching of basic science is extended into the last two years, in a manner which will permit a maximum of coordination with clinical teaching.
5. It will provide the faculty with an unprecedented opportunity to conduct continuing experiments in medical education. We need answers to many questions. What is the effect of starting the regular clerkships in the summer? How does the student respond to the basic science courses after he has had some clinical experience?

Realizing the importance of pursuing the experiment in medical education, the Board of Permanent Officers has created an Office of Associate Dean for Curriculum whose task it will be to supervise the curriculum from year to year and carry on a continuing effort to improve and coordinate the various parts of the curriculum. With the flexibility which has been introduced into the curriculum by the use of summers and the track system, the Associate Dean for Curriculum will have free sailing ahead.

The student is now the guinea pig of the experiment. We all hope it will succeed.

L.H.N.

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Predicting Coronary Heart Disease

It is easy to deal with a situation before symptoms develop—Lao Tzu.[1]

On the basis of a large number of epidemiologic investigations coronary heart disease (CHD) can now be predicted with greater assurance than any other disease, not only in population groups but also in individuals in terms of quantitative probabilities.[2] Of particular value in this regard to practicing physicians are two pieces of information. One is the risk ratio—that is the likelihood of a person developing clinical disease who has a group of risk factors as compared to others who do not have them. If a person has a constellation of risk factors, then it becomes possible to indicate the probability that a clinical disease will develop in an individual in a certain space of time.

Obviously it means much to know that one stands say one chance in four to become ill within the next ten years. And so a physician who advises an individual patient or evaluates the results of a screening program, requires quantitative data as a basis for preventive action. Present figures indicate that starting with 1,000 clinically healthy men then CHD will be manifested in 120 within ten years whereas the remaining 880 will be free of disease in these ten years. If the 120 of the 1,000 had a "positive" test result at the beginning of the ten years, and we knew what this "positive" test was we would have an ideal to strive for. However, the biology of man being what it is, it seems unlikely that a test of such predictive power will ever be be discovered. And so we have to settle for lesser accuracy.

CHD is now accepted as having multiple causes[3] and our interest attaches to the predictiveness of multiple risk factors first perhaps of two, serum cholesterol and blood pressure. On the basis of the Framingham study[4] persons with cholesterol levels over 260 mg. per cc. will develop CHD twice as commonly as people below this level. The implication of this finding is very great since we are now in possession of diets and medications which can greatly reduce cholesterol levels to below level of risk.

Identical information for elevated blood pressure levels are roughly parallel to that of cholesterol although a lower number.[5] The risk factors of blood pressure is 1:1.3. Taking both blood pressure and serum cholesterol elevation, then the predictive value of a positive test result is a little higher than for cholesterol levels alone. CHD becomes two and one-half times more likely with both risk factors in the upper range as compared with the situation where both risk factors are in the lower range. In the Framingham study no less than 42 per cent of all middle aged men were at increased risk on terms of one or the other or both of these risk factors. The ratio of risk is almost threefold which is a remarkable high figure and of much practical importance since high blood pressure as well as high cholesterol levels are amenable to successful medical management. Interestingly enough corresponding

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data from a different population—transport workers in London, in a different country are surprisingly similar.[6]

The more risk factors that are taken into account, serum cholesterol, blood pressure, left ventricular hypertrophy in the electrocardiogram, cigarette smoking, then the predictability of CHD increases, then it becomes distinctly higher than 1.3. A study of blood pressure, cholesterol levels and relative weight is not very accurate. But considering the above four risk factors then close to half developed clinical evidence of CHD within ten years. The general trend is clear the risk rises.

There are other factors which also operate as risk factors such as a personality type, B lipoprotein,[8] and even social class. This last, however, may reflect merely physical activity levels. All investigators recognize the difficulty of inferring from any such statistical type of analysis. However, the fact remains that the risk to which these men are exposed varies several fold and some of this gradient no doubt reflects a true causal relationship between the risk factors considered and the disease under consideration.

The data discussed above by Epstein[2] are impressive and represent the single most outstanding achievement of CHD epidemiology within the past years, all done at a tremendous effort and very great expense, but it is certainly worth the effort and expense. To be sure there are limitations to all the information so far presented such as smallness of numbers of cases involved, the wide range of CHD such as myocardial infarction, angina pectoris, electrocardiographic changes which makes individual epidemiology differ. The data also say nothing about so called minor ECG abnormalities such as T and ST wave changes and these matters must not be glossed over but constitute rather a basis for further intensive research. But we definitely have reached a point to apply in appropriate circumstances what is known rather than to use gaps in our knowledge as an excuse for inaction.

Although there is no proof that reduction in risk factor levels will reduce the toll from CHD the circumstantial evidence in favor of intervention to prevent premature disease is strong.[3] For we now have a rational background to screen susceptible individuals on the basis of quantitative assessment of preferential risk. In due course additional data will be available to improve prediction by including among the risk factors constituting a "positive test result' 'others such as physical inactivity, triglyceride levels, glucose tolerance and presumably biological influences as yet unknown.

In the meantime the remarkable predictive power of a series of tests has been documented and the figures speak for themselves. By means of two single measures alone, blood pressure and cholesterol levels, 40 per cent of middle aged men can be identified as being at risk three to five times more than the remaining 60 per cent. In approximately one man in four among those at preferential risk, CHD will develop within ten years. The added effect of other risk factors is also demonstrated. Pending the possible realization of the "ideal test" once the susceptibles have been identified there is need for early prevention. Lao Tzu had a prophetic word of advice, "it is easy to deal with a situation before symptoms develop."[1]

L.H.N.

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Anesthetics And Ventricular Performance

The anesthetist when planning suitable general anesthesia for a given patient always considers whether the drug or combination of drugs chosen may modify the contractile power of the heart. This is especially important in patients of extremes of age in whom drug responses are usually less predictable. The anesthetic care of patients has greatly improved since we have obtained a more thorough understanding of the effects of depressant drugs on ventricular function.

Three different techniques have been employed to clarify the physiological effects of anesthetics on ventricular performance. The Starling heart-lung preparation, measurement of maximal isometric systolic tension with a resistance strain gauge arch and establishing the relationship between stroke work and end-diastolic ventricular fiber length—the ventricular function curves.

The Starling preparation, of course, requires isolation of the heart and automatic denervation of the myocardium. It can give exact evidence of the direct effect of drugs on the myocardium. However, because it does not have the autonomic nervous system contribution to ventricular efficiency and reserve, the effects obtained by this technique cannot be interpreted in terms of how the intact heart would behave.

The strain-gauge arch gives maximal tension developed by a segment of the ventricular muscle. The changes measured are not isotonic but rather isometric. Applying the strain gauge arch is relatively easy and safe. The technique imposes only minimal interference with normal physiologic responses and these facts makes it particularly applicable for determining drug effects in man.

The ventricular function curves are used extensively to measure ventricular performance in animals but only to a limited extent in man because it requires the investigator to establish a relationship between ventricular stroke work and end-diastolic ventricular fiber length. The stroke work is calculated as the product of mean arterial pressure minus mean atrial pressure and ventricular stroke volume. The ventricular end-diastolic fiber length is expressed as either mean atrial filling pressure (atrial pressure minus intrapleural pressure) or as ventricular end-diastolic pressure. An increase in stroke work from a given end-diastolic ventricular fiber length represents improved ventricular performance. A decrease in stroke work when the fiber length is the same, indicated reduced ventricular performance. It is clear that such investigations require physiologic skill and sophistication. The measurements, however, like those obtained with the strain gauge arch are particularly helpful in clarifying the effects of various pharmacologic agents in intact animals and man.

Price and Helrich[1] tested cyclopropane, nitrous oxide and thiopental on ventricular performance with Starling's preparation. They found that at the same depth of anesthesia each reduced ventricular performance nearly equally. Halothane in concentrations greater than 1 per cent reduced ventricular performance also. Studies with the strain gauge arch showed similar decrease in heart contractile force except during the onset of light anesthesia. As anesthesia deepens ventricular performance decreased.[2]

While cyclopropane decreased ventricular performance in isolated hearts, the response in intact animals and patients was not uniform. In fact at times each drug improved ventricular performance. This means that while anesthetics depress ventricular performance primarily, this effect is antagonized by simultaneous action of catecholamines on the heart. The clinical inference here is obvious. Those patients whose sympathetic receptors in the heart are depleted by such drugs as reserpine and guanethidine are in actuality comparable to the Starling preparation, have lost their sympathetic contractile reserve and will show pure cardiac depression from anesthetic drugs. Flacke and Alper[3] points out that with respect to halothane, catecholamines are not augmented and the primary effect of the drug is to depress ventricular performance exactly as it does in the isolated heart.

Morrow[4] points out three clinically important conclusions which follow from the physiologic studies. All anesthetics tested can decrease ventricular performance. This decrease is related to the dose administered. Finally the net effect of drugs on ventricular performance may be modified by a simultaneous increase in circulating norepinephrine and epinephrine. It may be adversely modified if drugs such as reserpine have depleted the myocardium of its catecholamine stores.

Most importantly is the recognition that any anesthetic can be administered in such a way as to produce a severe reduction in ventricular performance.[5] In patients with cardiovascular disease and in patients at the extremes of age a relative overdosage can result if the anesthetic is administered too rapidly even though the dose or concentration used is within the usually accepted range. Viewing this knowledge objectively every physician is thankful to the trained anesthesiologist who with knowledge and skill stands guard over our patients during major operations.

L.H.N.

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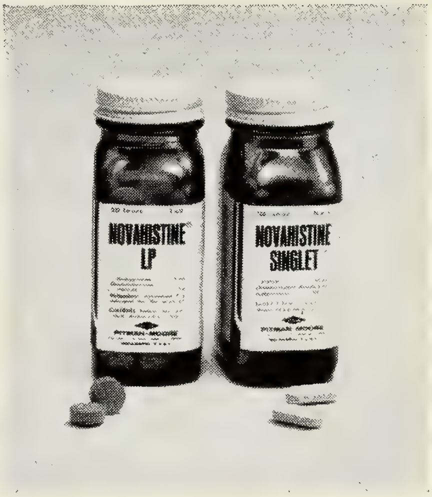

Obesity And Coronary Heart Disease

Studies of large populations have tended to show a relationship of weight to coronary heart disease (CHD). However, there is always the complicating factor that grossly obese patients have on the average higher blood pressure, higher serum cholesterol levels and higher incidence of diabetes. This has raised the suspicion that these factors are what may have been sampled in studies of the relationship between obesity and atherosclerosis.

It is to this problem that the Framingham group[1] have addressed themselves. They have analyzed in the last twelve years a sufficient number of persons in the population under surveilance and determined those who have developed CHD. Thus it has been possible to explore in more detail the independent contribution of body weight and weight change to the development of each manifestation of CHD. In these twelve years of observation, 252 men and 128 women developed CHD. There was a difference revealed between men and women in the clinical manifestation of this disease. In women, the predominant manifestation was uncomplicated angina pectoris. Men mainly developed the more serious lethal forms of the disease.

Another manifestation of CHD which proved strongly related to overweight was the occurrence of sudden death especially in men. The gradient of risk with increasing relative weight was steeper in men than in women especially in men with weight of 20 per cent or over above the median. Careful analysis further revealed that this increased risk was not due to musculoskeletal growth but to increase in adipose tissue. What can the mechanism of this relationship be?

In order to eliminate the factors of elevated blood pressure and serum cholesterol levels, they analysed obese men who had no elevation in blood pressure or serum cholesterol levels and found these males appeared to develop an excess of angina pectoris and sudden death. Another evidence of a unique effect of adiposity was the absence of its relationship to the risk of developing myocardial infarction which is well known as a manifestation of CHD strongly related to antecedent elevated levels of serum cholesterol and blood pressure.

What is comforting to the female sex is that adiposity had no effect in the absence of an elevated blood pressure or serum cholesterol. Only in those women presumably predisposed by elevation in these two risk factors was there present a possible excess risk among the obese.

There are several possible mechanisms both physiologic and metabolic in nature by which obesity could produce an excess of CHD. One is increased cardiac work load and blood pressure resulting from excess weight. Another might result from higher caloric intake and increased lipid levels and blood pressure accompanying gain in weight. A third might be a decrease in physical activity associated with obesity which might interfere with the development of collateral circulation in the hearts of subjects with existing atherosclerotic involvement of the coronary arteries. However, all of these factors enumerated could produce excess occurrence of myocardial infarction as well as angina pectoris and sudden death. This was not the case in the subjects of the Framingham study.

An increased cardiac work load in the obese appears necessary in order to maintain the increased O_2 supply demanded by the obese body. During exertion, an obese individual may require twice as much O_2 as is consumed by the normal individual under the same circumstances. Such an increased cardiac work load must be accompanied by an increased O_2 supply to the myocardium. An individual with a narrowed vessel lumen in the coronary system does not appear to be able to do this adequately. Thus if he is obese, myocardial ischemia and pain may occur when any added burden is placed on the heart. This is exactly what was found in the increased incidence of angina pectoris in the obese male patient.[2]

Besides the effect of obesity on circulatory dynamics, there are also mechanical disturbances caused by displacement of the heart by an elevated diaphragm, decreased respiratory excursion and the increased work required for breathing and moving about. This may result in a lowered vital capacity, ventilatory deficiency, increased oxygen debt and increased hematocrit values with increased blood viscosity. The view that there is an increased cardiac work load in obesity is sufficient to explain the findings reported by Kannel et al, without invoking the possible metabolic derangements which might also exist. It is apparent that subjects with comparable amounts of coronary atherosclerosis who are not overweight might tolerate an equal amount of physical exertion without developing angina

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pectoris since they lack the additional cardiac work load of obesity.

In subjects predisposed to atherosclerosis with an already compromised circulation the development of adiposity appears to precipitate attacks of angina pectoris or a fatal ischemia induced by arrhythmias that lead to sudden death. The question thus remains why obesity does not also precipitate myocardial infarction. Further studies in this area are desirable.

Avoidance of obesity because of its association with higher blood pressure and serum cholesterol levels would appear desirable in any preventive program designed to delay the onset of all manifestations of CHD. A program of weight reduction would presumably achieve a decrease in the level of these risk factors and at the same time decrease the cardiac work load and increase exercise tolerance. Avoidance of obesity would also decrease the risk of sudden death as well as incidence of angina pectoris.

It also follows logically that obese subjects suffering from myocardial infarction would have a harder time than normal weight subjects because of increased cardiac work necessary to supply the adipose tissue. It is a sort of permanent burden on a heart whose contractile power and cardiac output is already compromised. After recovery from the infarction obese subjects would very likely have improved exercise tolerance if they were induced to reduce weight. They would then develop less angina pectoris. In the same way subjects with established angina pectoris who are successful in reducing weight should exhibit improved exercise tolerance and a lower risk of sudden death.

L.H.N.

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A Physiologic Approach To Treatment Of Cardiogenic Shock

There are some patients who go into "cardiogenic shock" after an acute myocardial infarction (MI). These patients have hypotension and inadequate peripheral circulation. They all exhibit a low cardiac output. So also do patients in shock following sepsis hemorrhage and a variety of medical diseases. Since these latter cases of shock are not regarded as being cardiogenic, in what way is the mechanism of low cardiac output in non-cardiac cases different from that found after myocardial infarction. Is inadequacy of cardiac contractility the feature which distinguishes myocardial infarction shock from all the others?

It is true that many patients with shock after acute myocardial infarction do demonstrate impaired cardiac performance. Others, however, exhibit no abnormality of myocardial function at the time they are tested. In these latter patients a rapid infusion of dextran-40 restores normal cardiac output without any evidence of increasing the burden upon the heart. Right atrial pressure does not rise, pulmonary congestion does not develop and these findings indicate adequate left ventricular function.[1] A beneficial response to volume expansion in myocardial infarction shock has also been reported by others.

The salutary effect of volume expansion in some patients with myocardial infarction shock should not be too surprising. Measured blood volume is often found reduced particularly in patients with evidence of severe vasoconstriction. The sudden fall in cardiac output and arterial pressure which probably accompanies an acute MI may evoke reflex adrenergic discharge and vasoconstriction which may be sufficient to restore to normal or even elevate the arterial pressure above normal. The resulting vasoconstriction narrows the capacitance vessels increases capillary hydrostatic pressure and this leads to transudation of plasma out of the vascular spaces. It may also lead to trapping of red blood cells and plasma in areas of sluggish flow.

Cardiac filling may be temporarily augmented by the venoconstriction, but the end result of prolonged vasoconstriction is a reduction in circulating volume and a low cardiac output. Even if myocardial function now returns to normal as it may often do in a short time after infarction, cardiac output cannot increase until venous return is augmented. The level of peripheral resistance will remain usually high and the individual will exhibit cool, moist skin, rapid thready pulses. If, however, the patient with hypotension exhibits warm skin and slower pulses then the reflex vasoconstriction is not present and peripheral resistance will be

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1. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.

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found to be normal or even low. It is this second type of case, the patient with cardiogenic shock with low peripheral resistance which has led investigators for a search of vasodilator substances of cardiac reflexes which may inhibit adrenergic reflex effects, instead of increasing them.

A low cardiac output and hypotension without an elevated total peripheral resistance or tachycardia is not unique in patients with MI. A similar hemodynamic pattern has been observed in conscious dogs exposed to hemorrhage by Rushmer and has been described in human beings with other medical illnesses. It is, therefore, quite likely that individual differences in the pattern of cardiovascular response are at least partly responsible. "Low resistance" hypotension appears to be most common in patients with severe underlying diseases such as malignancy, diabetes, and cirrhosis in whom there is impaired adrenergic activity. There may be other factors such as heredity, age, stiffness of the vascular walls, which can affect the degree of vasoconstriction which will develop in a given individual.

These are some of the reasons why we might expect and actually do encounter a wide spectrum of responses in myocardial infarction shock, from the typical shock syndrome of intense calamitous vasoconstriction, to the clinical picture of hypotension and warm skin which many physicians may not even call "shock". Nevertheless these patients all have low cardiac output which may affect organ perfusion and lead to progressive circulatory deterioration unless combatted. The only difference between these types of cases may be the way their vascular systems have reacted to their stress.

If all patients with hypotension or inadequate blood flow after an MI are said to have "cardiogenic shock", the tendency might be to assume the mechanism is the same in all and that the therapy to be applied should be the same. However, it is now clear that mechanisms are different and therapeutic approach requires an understanding of the physiological derangements that need correction. Some patients who have intense vasoconstriction, cool, sweaty extremities and tachycardia with normal cardiac function and no heart failure will respond dramatically to plasma volume expanders like dextran-40.

Other patients without much reflex vasoconstriction, showing warm skin, not too rapid a pulse and hypotension are not reacting to their hypotension by reflex adrenergic response. In these patients infusion of a sympathomimetic vasoconstrictor agent like levophed may afford temporary circulatory support. Those patients whose primary fault is impaired myocardial contractility require treatment either with digitalis preparations, isoproterenol and if the situation is grave, even mechanical cardiac assistance.

Clearly the indications for each intervention requires a recognition of what is at fault in the causation of the shock and the response of the patient should be closely monitored to the point when the physiological faults have been corrected. Only by this physiological approach can we hope to significantly lower the present high mortality rate in patients with "cardiogenic shock".

L.H.N.

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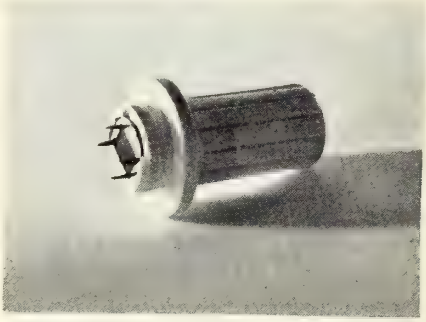

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Letters-to-the-Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Dear Dr. Nahum:

The Coroner-Medical Examiner relationship in Connecticut within the forseeable future it appears will undergo something resembling an upheaval and when things settle back there probably will be basic changes in it.

This idea is based on the fact the Connecticut Bar Association and The Connecticut State Medical Society—both groups of considerable prestige and some power in their respective fields—has a liaison Committee which, together with certain academic persons, has drawn up a bill which was introduced in the past Legislature to do away with the Coroner office entirely and replace it with a fulltime, salaried Chief Medical Examiner. Stripped of its traditional prerogatives the present Coroner duties would become functions of the States Attorney office, to eliminate present alleged duplications. The medical and quasi-medical features now practiced by our Coroner would then be assigned to the Chief Medical Examiner and the investigative duties which are presently done by the City or State Police, the County Detective, and the State Toxicologist, would be reported directly to the States Attorney office rather than being screened thru a Coroner first. To assuage the pains and the political wails which will arise with the decapitation of the office of Coroner, his position might well be moved into the office of the States Attorney where this new "Special Assistant" would concentrate on the preparation and trial of this type of case, with the same level of income—or better than at present—for his new duties. It is maintained that a full time, highly qualified, Chief Medical Examiner will do a much more efficient job with medical problems. The present part-time, local Medical Examiner, whose only real qualification is that he be a physician, is without prior special training and whatever skill he obtains from experience must be self-initiated.

For more than two decades the Connecticut Medical Examiner Association has tried to introduce a new system which would contain a Chief Medical Examiner to head up the medical aspects of the problem. This project started even before a survey was made by Professor Allan Morwitz of Western Reserve and Harvard, who designed and recommended a new system. When this proposal failed in the Legislature, the Section on Pathology of the C.S.M.S. tried its version and was unsuccessful, likewise. Now with the Bar, and some members of the Judiciary, interested in the problem and with a new medical school faculty aware of its position in the picture the problem has developed further.

One third of all deaths, approximately, should have, or already does have, some type of medico—legal investigation Besides the classical causes of accidental, suicidal and homocidal death and those of persons found dead, or dead by "natural causes" but unattended, or due to negligence or carelessness on the part of others, new features more widely accepted now than even ten years ago include the problems of the Workmens Compensation laws, and some other insurance matters, but also those related to public health and general welfare in wider coverage. This is an area in which practical medicine and practical law come into intimate contact. The present relationship stretches back to the laws of 1883 and the vast increase in the amount of medical knowledge of the past eight-five years, and its application in this regard, is not perhaps always so fully utilized as it should be. The office of Coroner persists here even though it has been abandoned in our surrounding States. In fact about one third of all states in the Union have abandoned the office of Coroner and replaced it by a Chief Medical Examiner, or his equivalent.

As the problem today presents itself it might be said to offer a choice. One suggestion is that the Coroner stop practicing medicine, that his powers on the legal side be further deleted even beyond what they recently have been, until he is cut down to the position of a screener only, and that in this weakened position he carry on while the Medical Examiner has been "beefed up". That appears to be an intolerable position—for both. However, the second suggestion that the Coroner retain all his present powers and a medical-legal expert, a Professor of medico-legal Pathology at the new Medical School be retained as a "consultant" to the local Medical Examiners, Certified Pathologists, Coroners, Police, States Attorney, etc., has one cardinal weakness: it is most unlikely since there are so very few of them available in the entire country, or are being trained for the future, that any acceptably qualified medico-legal pathologist would consider such a post. A number, a small number questioned about such a position, have evidencel no interest in it, consider it demimonde. To obtain a fully trained medico-legal expert to head up a modern investigative system in this State a position of Chief Medical Examiner apparently must be offered full powers and full responsibilities and full salary.

Should a Chief Medical Examiner, with proper assistants, a certified panel of Pathologists, and a group of trained, local Medical Examiners be engaged by a Commission appropriately appointed for that specific purpose the expenses of these offices should be furnished from a budget of this Commission. It should be separated from both the Judiciary and the Police—as it has so successfully been done in many of the States, both along the Atlantic seaboard, as well as the mid and far West. An appropriate proportion of his total salary could be assumed by the Board of Trustees of the Medical School for teaching duties.

At this time such a concept seems a reasonable solution of this problem that has bothered the State of Connecticut for the past forty or fifty years.

Brae Rafferty, M.D.
807 Main Street, Willimantic, Connecticut

To The Editor:

1968 marks The Gaylord Hospital's 65th year of medical service to the citizens of our State.

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In the interests of better informing the physicians of our State as to the medical services provided Connecticut residents by Gaylord, we respectfully request this letter's publication in the *Connecticut State Medical Journal.*

The Gaylord Hospital
Wallingford, Connecticut

Thomas F. Hines, M.D.
Medical Director

Doctor's Office

Irwin Broudy, M.D., announces the opening of an office for the practice of adolescent and adult psychiatry at 881 Lafayette Street, Bridgeport.

Samuel J. Janet, M.D., announces the relocation of his office for the general practice of medicine to 89 Broad Street, Milford.

Charles Ray Jones, M.D., announces the opening of an office for the practice of pediatric oncology at 2508 Whitney Avenue, Hamden.

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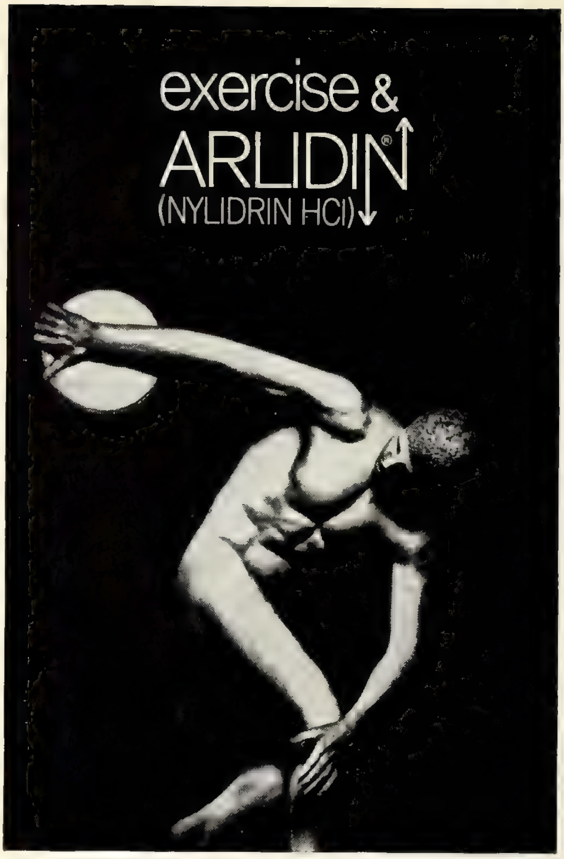

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April 30, May 1, 2, 1968

PRELIMINARY PROGRAM

TUESDAY, APRIL 30

MORNING SESSION

8:00 Registration of Delegates—Mezzanine Floor
Continental Breakfast

9:00 Call to Order—Opening Session—House of Delegates—Terrace Room

12:30-1:30 Luncheon for Delegates and Official Guests—City Rooms

AFTERNOON SESSION

12:30 Registration for Scientific Program—Mezzanine Floor
Opening of Exhibits—Ballroom—Mezzanine Floor

TERRACE ROOM

1:30 Call to Order—President of the Society
Address of Welcome—President-elect of the society

1:45 Future and Present Concepts of Population Control
Sheldon J. Segal Ph.D., *New York City;* Director, Biomedical Division, Population Council, Rockefeller University, New York

2:45 Discussion
John McLean Morris, *New Haven,* Professor of Gynecology, Yale University School of Medicine, New Haven

3:00 Reference Committee Hearings--House of Delegates

3:30 Section Meetings
Section on Internal Medicine
Section on Pediatrics
Section on Radiology
Association of Medical Examiners of Connecticut

EVENING SESSION

6:30 Reception and Dinner for Delegates and Official Guests
City Rooms—Mezzanine Floor

8:00 Program by CSMS Committee on Medicine and Religion—Terrace Room

PRELIMINARY PROGRAM

WEDNESDAY, MAY 1

MORNING SESSION

9:00 Registration for Scientific Assembly—Mezzanine Floor

TERRACE ROOM

Symposium on Atherosclerosis

Moderator: Philip K. Bondy, New Haven; Professor Medicine, Yale University School of Medicine

9:30 A Further Report From the Framingham Study
William B. Kannel, *Framingham, Massachusetts*;
Medical Director, National Institute of Health,
Heart Disease, Epidemiology Study, Framingham

10:15 Biochemical and Clinical Aspects of the Hyperlipidemias Associated With Accelerated Atherogenesis
Robert S. Lees, *New York City*; Assistant Professor and
Associate Physician, Rockefeller University, New York

11:00 Intermission to Visit Technical Exhibits

11:30 New Concepts in the Evaluation of Human Obesity and its Relationship to Disordered Carbohydrate and Lipid Metabolism
Lester B. Salans, *New York City;* Assistant Professor and
Associate Physician, Rockefeller University, New York

12:15 Panel Discussion
Moderator: Philip K. Bondy
Panelists: William B. Kannel, Robert S. Lees, Lester B. Salans

1:00 Luncheon—City Rooms
Intermission to Visit Technical Exhibits

AFTERNOON SESSION

2:00 Section meetings
Section on Dermatology
Section on Gastroenterology
Section on Obstetrics and Gynecology
Section on Ophthalmology
Section on Physical Medicine and Rehabilitation
Section on Urology
Connecticut Diabetes Association

3:30 Final Session of House of Delegates—Terrace Room

7:00 Reception—Mezzanine

8:00 Annual Dinner—Dancing—Terrace Room

PRELIMINARY PROGRAM

THURSDAY, MAY 2

MORNING SESSION

9:00 Registration for Scientific Assembly—Mezzanine Floor

TERRACE ROOM

9:30 Symposium on Medical Genetics
Moderator: Herbert A. Lubs, New Haven; Assistant Professor of Medicine and Pediatrics, Yale University School of Medicine, New Haven

Panel: Alfred Knudson, *Stony Brook, New York*: Professor of Medicine, Health Sciences Center, Stony Brook, New York
Leon E. Rosenberg, *New Haven*: Assistant Professor of Medicine and Pediatrics, Yale University School of Medicine

11:00 Intermission to Visit Technical Exhibits

11:30 New Concepts in the Treatment of Medical Shock
Roman DeSanctis, *Boston;* Assistant Physician Department of Medicine, Massachusetts General Hospital, Boston

12:15 New Concepts in the Treatment of Surgical Shock
Stanley M. Levenson, *Bronx, New York*; Professor of Surgery, Albert Einstein College of Medicine, Yeshiva University, New York

1:00 Luncheon—City Rooms
Intermission to Visit Technical Exhibits

AFTERNOON SESSION

TERRACE ROOM

2:00 Transplantation:—A Modern Perspective
(Arranged with Connecticut Society of American Board Surgeons)

3:30 Section Meetings
Section on Allergy
Section on Anesthesia
Section on Neurology
Section on Neurosurgery
Section on Orthopedics
Section on Otolaryngology
Section on Pathology
Section on Proctology
Connecticut District Branch American Psychiatric Association
Section on General Practice
Connecticut Society of American Board Surgeons

Foreword

This issue of *Connecticut Medicine* is devoted to cardiac problems: particularly advancements in the delivery of medical care, clinical application of research, and new ideas in cardiology for practicing physicians in the State of Connecticut.

Dean T. Mason, M.D., Chief of Cardiovascular Diagnosis, National Heart Institute, Bethesda, has been Visiting Professor in Post-graduate Medical Education in central Connecticut annually for several years. His clinical acumen, his interest in basic research, his fundamental background in basic research and his overwhelming interest in bringing to the practicing physician knowledge gleaned from the laboratory are obvious in his article on the application of basic pharmacology to clinical cardiology. The foxglove has been used for 300 years, since the days of Withering, nitroglycerine and quinidine for about 100 years, all on an empiric basis. Now, for the first time, we get some understanding of the mechanisms by which these medications are beneficial to our patients.

It is almost incredible that myocardial infarction was recognized as a clinical entity only 50 years ago, within the life time of most of the readers of this *Journal.* Even more incredible, only in the past one or two decades has it been recognized as the most common cause of death in the United States, and only in the past few years, have concerted efforts been made to reduce its alarmingly high mortality.

Dr. Victor Estaba reminds us of a simple test to differentiate "angina" due to esophageal disease from angina due to coronary artery disease.

Experience in a coronary care unit, pioneered in New Haven by Dr. Oscar Roth, is reviewed in this issue. Every modern hospital of moderate size should have a coronary care unit. The information outlined in this article should be of interest to all practicing physicians.

In caring for patients with myocardial infarction, successful resuscitation after cardiac arrest has been a gratifying experience to any physician who has been involved. Such patients literally have been brought back from the "edge of the grave". The article by Dr. Robert M. Jeresaty documents experiences in a major Connecticut hospital, using modern resuscitation techniques. It should serve as a model for us all.

Electrocardiograms, in the recent past, were ordered only when specifically indicated. Now, a patient is seldom allowed to go to surgery, nor is any physical examination considered complete, without an electrocardiogram. Physicians who read electrocardiograms are flooded with "routine" electrocardiograms. How to cope with this modern development in medicine is the subject of the article by Dr. Robert Dobrow, who reports on computer applications to solving this problem.

Thus, this issue of *Connecticut Medicine* serves as a bridge, from the past, to the present, to the future; providing the practicing physician with an understanding of some therapy previously inexplicable, cataloguing some therapy previously unavailable, and providing a glimpse into the future for management, therapy and understanding of pharmacodynamics and therapy which, relatively recently, seemed unobtainable.

Morris J. Seide, M.D.
Guest Editor

Clinical Significance Of Recent Advances In The Pharmacology Of Cardiovascular Drugs

Dean T. Mason, M.D.

In spite of the fact that digitalis, quinidine, and nitroglycerin are the most important drugs for the treatment of cardiac disease and have been available to physicians for many years, their salutary clinical actions have been firmly established only on an empirical basis and their mechanisms of action have not been well understood. However, several recent studies have contributed considerably to our knowledge of the pharmacology of drugs acting on the heart, and since a thorough appreciation of the pharmacodynamics of these agents forms the cornerstone of a sound practice of cardiology, it is the purpose of this presentation to examine in clinically important terms our present knowledge of these drugs. In addition, the newly introduced therapeutic agents, beta-adrenergic receptor blocking drugs, are evaluated. In this review, no attempt is made to describe and substantiate complex investigational procedures but rather to focus attention on certain practical concepts, deduced from basic and applied studies, which are applicable to the use of these drugs in patients.

Digitalis

The only direct effect of digitalis of clinical importance is its ability to stimulate myocardial contraction. The many beneficial actions resulting from its use are derived from this fundamental property and, in this manner, the altered hemodynamics characteristic of the heart failure state are restored towards normal. The contention, held in the past, that these agents improve the circulatory state by a direct action on the kidney, sinoatrial node, or the venous bed is no longer tenable. In the failing heart, there is incomplete emptying of the ventricle during systole, resulting in an abnormal elevation of ventricular pressure in end-diastole. Since digitalis stimulates the contractile state of the heart, ventricular function is improved so that at any given end-diastolic pressure, more nearly complete systolic emptying occurs, leading directly to the enhancement of the lowered stroke volume and cardiac output, and indirectly to the reduction of the elevated ventricular end-diastolic and venous pressures and to the diminution of the increased peripheral vascular resistance and heart rate (Fig. 1). It is important to emphasize that the major effects of digitalis on cardiac rate in heart failure are indirect and result from reduction of the reflex sympathetic stimuli to the sinoatrial node. Although the drug in high doses has a slight effect on sinus pacemaker activity through stimulation of the vagus nerve, this action is of little clinical importance in therapeutically useful doses. For these reasons, digitalis is of little value in slowing sinus tachycardia in the absence of heart failure.

Although it is acknowledged that the glycosides stimulate the failing heart, there has been considerable confusion concerning the effects of these agents on the contractile state of the normal heart. Since the drug reduces the cardiac output in normal subjects, it has been postulated that digitalis depresses the function of the heart. However, it is now recognized that the cardiac output may be altered by certain extracardiac factors and thus alone does not necessarily provide an assessment of cardiac contractility. A more critical evaluation of this problem has shown quite clearly that these agents augment myocardial contraction both in patients with heart disease without failure and in normal subjects (Fig. 1). Thus in these patients, the drug increases the rate at which intraventricular pressure and tension rise during contraction[1] and augments the velocity of ventricular shortening during systolic emptying[2]. Since digitalis has the same fundamental action on both normal and failing hearts, the view that the drug has a harmful effect on the nonfailing heart can not be given credibility. Digitalis lowers the oxygen debt following exercise in patients with cardiomegaly but without heart failure, indicating that the functional

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DIGITALIS
Actions on Circulatory Dynamics

	Normal	Congestive Heart Failure
Heart rate	↓	⬇
Arterial pressure	↑	⬆
Cardiac contractility	↑	⬆
Cardiac output	↓	⬆
Stroke volume	↓	⬆
Systemic vascular resistance	↑	⬇
Venous pressure	↑	⬇
Venous tone	↑	⬇
Venous return	↓	⬆
Splanchnic blood volume	↑	⬇
Total blood volume	=	⬇

↑ Small increase ⬆ Large increase
↓ Small decrease ⬇ Large decrease
= No change

Figure 1. Actions of digitalis on circulatory dynamics in normal subjects and patients with congestive heart failure.

status of the circulatory system may be improved by the drug in at least some patients without overt heart failure[3]. In addition, digitalis may be of potential clinical value in preventing the development of ventricular hypertrophy in patients with aortic valvular disease or hypertension without heart failure, since the drug reduces the degree of mortality from heart failure and the degree of ventricular hypertrophy resulting from a chronic pressure load in experimental animals[4]. Further, the belief that the administration of digitalis in special situations may be helpful in certain cardiac patients without failure is gaining in prevalence. Thus, prophylactic digitalization may protect the myocardium in these patients in the face of the depressing effects of anesthesia and operation, serious illnesses such as pneumonia, and the hypervolemic state during pregnancy.

Although it is agreed that the therapeutic actions of the digitalis glycosides are primarily a result of their cardiotonic properties, considerable evidence now exists to indicate that these agents have important peripheral vascular actions as well. It has been shown in normal subjects that digitalis constricts the arterial and venous beds of the systemic circulation by a direct stimulating action[5] (Fig. 1). These extracardiac vascular actions of the drug may explain, in part, the failure of the drug to augment the cardiac output in patients without cardiac decompensation in spite of the fact that the glycoside clearly increases myocardial contractility. The increased resistance to ventricular ejection would tend to offset the augmented force of cardiac contraction. Further, although venoconstriction throughout the entire systemic venous bed would tend to shift blood towards the central circulation, there is evidence even in man, however, to suggest that this venoconstriction is more intense in the hepatic veins, resulting in portal venous pooling and ultimately diminished venous return to the heart. In contrast to normal subjects, in patients with heart failure, the glycoside lowers the elevated forearm vascular resistance and venous tone towards normal[5] (Fig. 1). Since the peripheral vasoconstriction in patients with heart failure is produced by increased activity of the sympathetic nervous system, the reason for the opposite effects of the drug on arteriolar resistance and venous tone in these patients and normal subjects is that the elevation of cardiac output induced by digitalis in patients with heart failure results in a diminution of this adrenergically induced vasoconstriction. This vasodilatory action is indirect and overrides the direct stimulating effect on the peripheral blood vessels observed in normal subjects. Thus, the effects of the glycoside on the peripheral vascular beds are dependent on the circulatory state of the patient at the time the drug is administered. The finding that digitalis results in systemic venodilation in patients with heart failure provides an explanation for the clinical observation that digitalization of these patients results in a fall in systemic venous pressure before the onset of diuresis. In spite of the overall venodilation and reduced central venous pressure following the drug in heart failure, venous return is actually augmented due to a shift of blood in the portal venous reservoir to the systemic venous bed. In addition, the digitalis-induced cardiotonic action provides a more forceful ventricular contraction from a relatively lower filling pressure, resulting in marked enhancement of cardiac output.

The electrophysiologic actions of digitalis on the myocardium are complex and in general are mediated by a combination of vagal, anti-adrenergic, and direct effects. Of importance in the genesis of premature extrasystoles and ventricular tachycardia is that the drug augments cardiac excitability and increases automaticity or ectopic pacemaker activity through an increase in the slope of diastolic depolarization (Fig. 2). In high doses the agent prolongs depolarization by reducing the rate of rise of

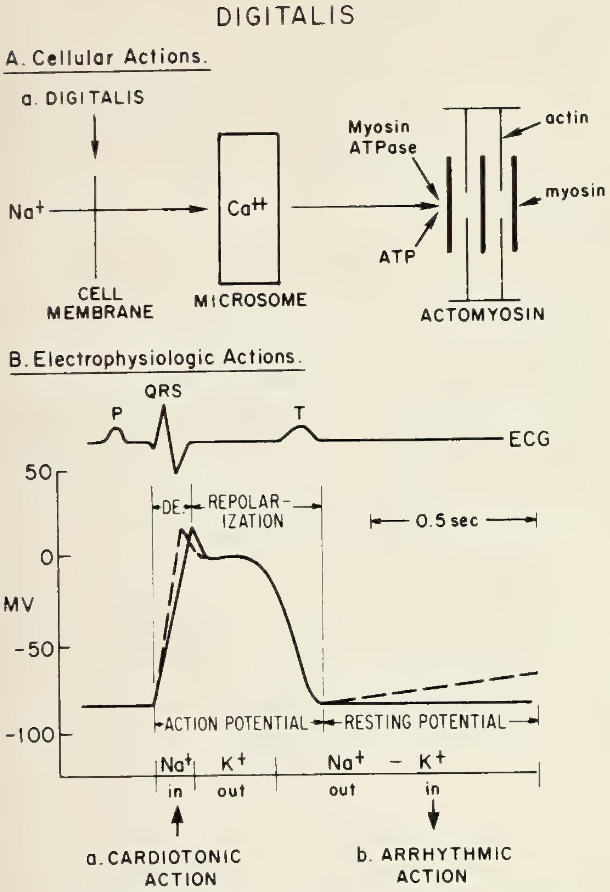

Figure 2. Proposed cellular (A) and electrophysiologic actions (B) of digitalis. A. Schematic diagram demonstrating events within the cardiac muscle cells. Presumably digitalis influences a cell membrane ATPase to increase intracellular sodium (Na^+), which enters microsomes where it releases calcium (Ca^{++}), thereby initiating contraction by providing calcium for the contractile protein actomyosin (actin plus myosin). a. Indicates the point at which digitalis initiates its cardiontonic action. ATP = adenosinetriphosphate. B. Schematic diagram representing the relationship between the electrocardiogram (ECG), the intracellular electrical events in ventricular tissue, and transmembrane alterations of intracellular and extracellular cation concentrations. Depolarization (DE) is accompanied by a shift of sodium into the cell and a sudden rise in potential (spike action potential). In the early portion of repolarization potassium (K^+) leaves the cell. During the latter phase of this period the potential falls to the level of the diastolic resting potential, a process mediated by the return of potassium into the cell and sodium from the cell. a. Digitalis exerts its cardiotonic action by augmenting (↑) the amount of sodium which enters the cell and presumably accelerates the rate of rise of the spike action potential and conduction velocity (dashed line on the left). b. The drug produces its ectopic arrhythmic action by inhibiting (↓) the sodium-potassium pump mechanism during diastole, resulting in less efficient maintenance of sodium outside and potassium within the cell. Thus, gradual intracellular accumulation of sodium and loss of potassium occurs, the resting potential slowly rises to produce diastolic depolarization (dashed line on the right), actions which underlie the ecotopic pacemaker activity of the glycoside.

the spike action potential, resulting in an increased PR interval and more advanced atrioventricular block. There is one direct action of digitalis of therapeutic importance other than its aforementioned action on cardiac contractility; the ability of the drug to prolong the functional refractory period of the atrioventricular node. Since the refractory period of this cardiac tissue determines the rate at which stimuli from supraventricular pace makers are transmitted to the ventricles, this action of the drug is useful in slowing the ventricular rate in patients with atrial fibrillation. In contrast to its effects on the atrioventricular node, digitalis shortens the refractory period of atrial and ventricular myocardium, a property which contributes to the genesis and perpetuation of ectopic rhythms.

The fundamental mechanism by which the cardiotonic actions of digitalis are mediated by the myocardial contractile machinery is still largely speculative but recent knowledge concerning the structure of heart muscle and the processes involved in normal contraction have provided new insight into this important problem[6]. At the time of depolarization, indicated by the onset of the QRS or spike action potential, sodium enters the cell followed by a loss of potassium (Fig. 2). The microsomes of the sarcoplasmic reticulum take up the sodium and, in turn, release calcium to the contractile protein, actomyosin. In the presence of ATP produced from mitochondria and the enzyme, myosin ATPase, contraction is activated within the sarcomere or basic structural unit of the myofibril, resulting in sliding together of the thin actin filaments and overall systolic shortening of the ventricle. During repolarization sodium is actively pumped out and potassium is pumped into the cell in order to restablish the characteristic cation concentration on either side of the cell membrane. Present evidence now indicates that digitalis in therapeutic concentrations affects this excitation-contraction response by stimulating a certain enzyme ATPase within the cell membrane which actively transports sodium into the cell at the time of depolarization, thus ultimately providing a greater quantity of calcium for the contractile process, and a more forceful contraction[7] (Fig. 2). Also, it appears that digitalis stimulates a relaxing factor which removes calcium from the active contractile sites and results in a shortening of the period of contraction. As the dose of digitalis is increased, there is inhibition of another membrane ATPase, that of the sodium-potassium pump mechanism operative during depolarization and the period of the diastolic resting potential. In this manner, active transport of sodium out of the cell and potassium into the cell is hindered; sodium influx is enhanced while potassium leaks from the cell (Fig. 2). From these observations it is postulated that there are two membrane receptors for digitalis, one that is stimulated during depolarization by doses employed clinically for the cardiotonic action of the drug, while the other is depressed during the later phase of the electrophysiologic cycle by larger and more toxic doses and results in the appearance of diastolic depolarization and a tendency for spontaneous ectopic beats. This hypothesis that digitalis alters the active transport of cations at the cell surface without entering the intracellular space is consonant with electron microscopic studies which have shown that radioactive digitalis is localized within the cell membrane structure of the sarcoplasmic reticulum[8]. Further, since the cell membrane makes deep invaginations into the cell, the drug may come in close contact with the many myofibrils within the cell without actually leaving the interstitial medium.

A working knowledge of the intracellular processes underlying the actions of digitalis is helpful in the clinical use of the drug since it has been implied that the cardiotonic and arrhythmia-producing effects of digitalis are mediated by different mechanisms. Indeed, it has been demonstrated that in the intact organism these two properties of the drug may be dissociated by the administration of potassium[9]. Thus, the suppression of digitalis toxicity by the action of potassium which reduces the automaticity of idioventricular pacemaker activity does not antagonize the positive contractile actions of the glycoside. Translated into a clinical setting, it is clear that in a patient with heart failure undergoing rapid diuresis, the administration of potassium to protect against the development of ventricular extrasystoles would not counteract the cardiotonic action of digitalis. In addition, since the production of digitalis-induced extrasystoles is accompanied by the loss of intracellular potassium, a basis is established for the administration of potassium to counteract these arrhythmias brought on by the glycoside. However, potassium loss is not related to the other toxic actions of digitalis. In fact, potassium treatment is contraindicated in the presence of digitalis provoked atrioventricular block, since both digitalis and potassium diminish conduction velocity. Importantly, it now appears that the relationship between the dose and the positive actions of digitalis on contracile force is essentially linear[9]. Small doses of digitalis have the same effect as large doses proportional to the dose employed. Therefore, a patient need not receive the total digitalizing dose in order to obtain a therapeutic effect; rather, small amounts of the drug provide some beneficial action, a point worthy of consideration if the drug is administered to a patient prone to digitalis intoxication or if the drug is employed prophylactically.

Until recently there has been the notion that the digitalis glycosides improve the contractility of the heart without increasing myocardial oxygen consumption, a view that implies the drugs possess a unique ability to improve the efficiency of the heart by producing mechanical work without utilizing chemical energy. Keeping in mind that myocardial oxygen requirements are elevated by a rise in the velocity of contraction, as well as by an increase in the size of the heart and the tension developed by the myocardium, reevaluation of the important question concerning the effects of cardiac glycosides on myocardial oxygen consumption in the non-failing heart has indicated a different interpretation from the traditional concept; digitalis increases markedly the velocity of myocardial shortening while the size of the non-failing heart is decreased minimally[10]. Therefore, the drug has the direct effect of actually augmenting the oxygen consumption of the heart and diminishing cardiac efficiency. Thus, the beneficial cardiotonic action in the non-failing heart is produced at the cost of a disproportionally large increment of energy utilization. However, in the enlarged and failing heart, this direct effect is overridden by the marked fall in ventricular end-diastolic volume and systolic wall tension, resulting in an overall decline of myocardial oxygen utilization and an increase in efficiency[10]. From these considerations, it is interesting to postulate that the beneficial actions of digitalis in the treatment of angina pectoris results from the improvement of impaired performance of the heart by reduction of the size of the heart and wall tension; in a patient without at least some degree of cardiac impairment the drug might actually intensify anginal symptoms.

Finally, it has recently been demonstrated that certain alterations of the humoral background in which digitalis is administered may modify the actions of the drug. Although reserpine interferes somewhat with the cardiotonic actions of digitalis, it does so aside from its norepinephrine depleting properties[11]. Thus, the presence of cardiac norepinephrine stores are not necessary for the full cardiotonic action of digitalis, and the cardiotonic actions of digitalis are additive to those of the catecholamines and to drugs which act through the release of endogenous norepinephrine. Further, the complete stimulating effect of digitalis can be anticipated in the presence of beta-adrenergic receptor blockade and other types of anti-adrenergic drugs other than reserpine. Although the cardiotonic actions of digitalis are not influenced by alterations of myocardial catecholamine content, norepinephrine depletion or beta-adrenergic receptor blockade reduces the incidence of digitalis-induced ventricular arrhythmias. Also, a major portion of the ability of the glycoside to prolong the functional refractory period of the atrioventricular node is dependent on autonomic innervation[12]. The level of thyroid activity can modify the actions of digitalis[13]. The hypothyroid state augments the cardiotonic actions, the arrhythmia-provoking properties, and the effect of lengthening the refractory period of the atrioventricular node; the hyperthyroid state tends to alter these responses in the opposite direction.

Quinidine

Although there are a number of substances that have been employed in the management of disorders of cardiac rhythm, quinidine has been the most important drug for the clinical treatment of these disorders and might be considered to be the prototype of the antiarrhythmic agents. At the onset of this section it can be stated that what will be said of quinidine is also true for procaine amide and that for clinical use, allowing for difference in dose, and toxic actions on the central nervous system and gastrointestinal tract, the two agents are equally effective in the treatment of atrial and ventricular arrhythmias.

The mechanisms responsible for the genesis of cardiac arrhythmias are complex and not completely defined. However, there is general agreement that atrial and ventricular extrasystoles and atrial paroxysmal tachycardias are attributable to ectopic pacemaker activity discharging irregularly or rhythmically; and that atrial and ventricular fibrillation and ventricular tachycardias result from circus impulse movement of the reentry or reciprocal excitation type, initiated by a premature beat. Thus, certain features such as the rate of ectopic pacemaker discharge, the duration of the refractory period, the conduction velocity, and the excitability of cardiac tissue are crucial to the perpetuation of arrhythmias. Quinidine exerts its beneficial arrhythmia-depressing actions by modifying these electrophysiologic properties of the heart[14] (Fig. 3). Although quinidine has several effects on the electrical events within the cell which are of potential benefit in reverting disorders of cardiac rhythm, the most important action in this respect is that the drug directly prolongs the effective refractory period of the myocardium. This conclusion is based on the fact that a significant prolongation of the effective refractory period of atrial and ventricular muscle occurs with doses of quinidine which affect conduction velocity, excitability, and the rate of ectopic pacemaker activity to a lesser degree. Thus, repetitive ectopic impulse formation is abated as a result of the impulse firing into surrounding tissue that is completely refractory. In intact man, the effects of quinidine on the refractory period are complex and result from direct and anticholinergic actions of the drug. Since vagal stimulation shortens the refractory period of atrial muscle, increases that of the atrioventricular node, and has no effect on ventricular muscle, the overall effect of the drug is to prolong this period markedly in the atria, increase it mildly in the ventricle, and to decrease it in the atrioventricular node. As a result of this effect on the atrioventricular node, the ventricular may be accelerated when the drug is administered alone to patients with atrial fibrillation. The ability of quinidine to prolong directly the refractory period is attributable, in part, to its action of increasing the duration of the total action potential. In addition, the functional refractory period is prolonged for a short interval after restoration of the resting membrane potential, and therapeutic concentrations of the drug may prolong the refractory period with little or no prolongation of the action potential.

In regard to the other electrophysiologic properties of quinidine, the drug reduces normal and ectopic pacemaker activity by diminishing the slope of diastolic depolarization (Fig. 3). Importantly, the ability of quinidine to depress spontaneous diastolic depolarization is more pronounced on ectopic pacemakers than on normal pacemaker cells. Although the direct effect of the drug is to depress impulse formation in the sinoatrial node, in the intact organism the vagolytic action usually predominates, resulting in no change or a slight acceleration of heart rate in patients with normal sinus rhythm. Quinidine decreases the velocity of impulse conduction by reducing the rate of rise of

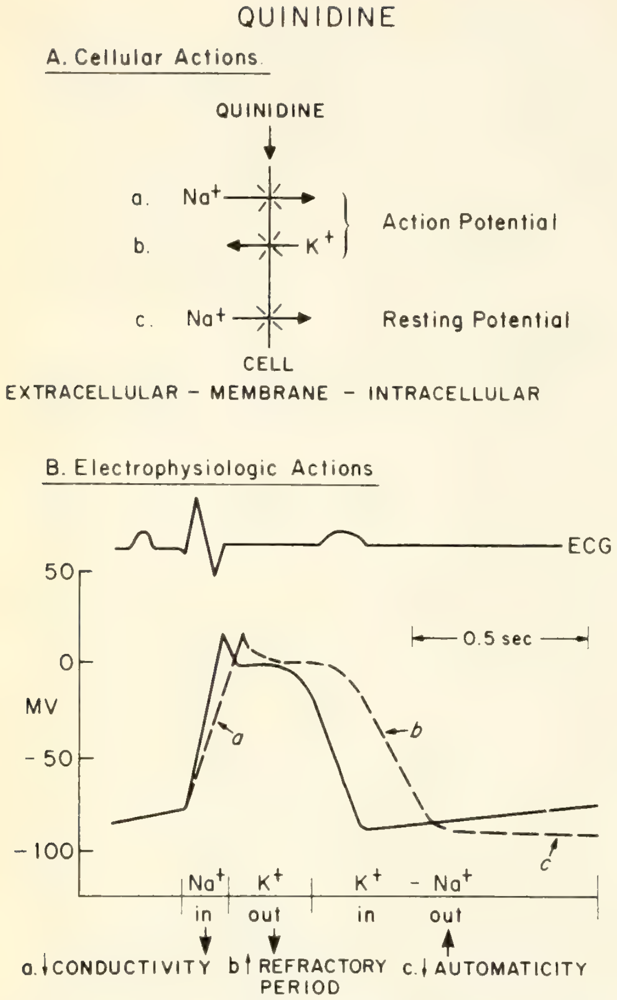

Figure 3. Proposed cellular (A) and electrophysiologic actions (B) of quinidine. A. Schematic diagram demonstrating the action of quinidine on the cell membrane of heart muscle. During the time of the action potential, the drug impedes (X) the inflow of sodium and diminishes (X) the extrusion of potassium from the cell. During the resting potential the influx of sodium is hindered (X). a. Indicates the diminished shift of sodium responsible for the negative cardiotonic action and reduction of conductivity produced by quinidine. b. Shows the reduced efflux of potassium related to the prolongation of the duration of the action potential and refractory period. c. Indicates the inhibition of the transmembrane movement of sodium related to the quinidine-induced depression of automaticity. B. Schematic diagram representing the same relationships as shown in Fig. 2B for ventricular muscle, except that ectopic diastolic depolarization is depicted in the control state in the present figure. The actions of quinidine on electrical activity are shown by the dashed line. Quinidine results in (a) a decrease in conductivity, accompanied by a diminution (↓) of sodium influx into the cell and a decline of the rate of rise of the spike action potential; (b) an increase in the duration of the refractory period, associated with a decrease (↓) in potassium efflux from the cell and an increase in the duration of the action potential; and (c) a decline in automaticity which is related to a reduced sodium influx into the cell (or increased sodium efflux: ↑) and an abolition of diastolic depolarization.

the spike action potential, thereby prolonging depolarization and resulting in widening of the QRS complex and various degrees of atrioventricular block. Although the threshold to electrical stimulation is increased by quinidine, this action of the drug is probably not of major significance in clinically useful doses. It should be remembered that the drug lowers arterial pressure by reducing cardiac output as a result of a decrease in myocardial contractility and as a result of a direct dilator and anti-adrenergic effect on vascular smooth muscle.

It has been postulated that the electrophysiologic and contractile actions of quinidine are mediated by alterations of the flow of cations across the cell membrane produced by the drug[14] (Fig. 3). Quinidine is thought to bind to lipoprotein in the cell membrane, resulting in decreased membrane permeability to the movement of cations. In this manner, the entrance of sodium into the cell is reduced during the period of the resting potential. Thus, diastolic depolarization is suppressed, accounting for the action of quinidine in reducing automaticity of normal and ectopic pacemaker cells. In addition, the drug reduces sodium influx during depolarization, an action that may underlie the drug's negative cardiotonic effect and its slowing of impulse conduction. Also, during repolarization there is diminished efflux of potassium which is thought to be related to the augmentation of the duration of the refractory period.

It is of interest to compare the opposing cellular effects of digitalis and quinidine. Both drugs appear to be capable of exerting their therapeutic actions without necessarily entering the cell itself. However, it is postulated that digitalis augments contractility by increasing sodium movement into the cell and quinidine reduces contractility by the opposite action. It is implied that the drugs are not working on the same mechanism; digitalis is stimulating a membrane enzyme, while quinidine supposedly repels sodium influx as a consequence of the positive charge on its molecule. Digitalis induces its automacity-enhancing actions by interfering with the membrane enzyme system for keeping sodium out and potassium within the cell during diastole. In contrast, quinidine depresses automaticity by preventing sodium influx, but apparently does so by the action of the charged drug itself and not through an enhancement of pump enzyme activity. Thus, although the drug has a beneficial effect in preventing digitalis induced extrasystoles in certain patients, quinidine is not a specific antidote for digitalis intoxication.

Nitroglycerin

The organic nitrate, nitroglycerin (glyceryl trinitrate), is the most important of the nitrite drugs which also include the organic nitrites and the inorganic nitrite ion. In the past, there has been much confusion concerning the effects of the various nitrite compounds, but it is now clear that they all possess one and the same fundamental property, vasodilation in nearly all of the regional circulations. This relaxing effect on vascular smooth muscle is produced by the direct action of the drugs; the vasodilation is not blocked by anti-adrenergic drugs but may be antagonized by vasopressor agents. When the nitrites enter the circulation slowly, such as following sublingual nitroglycerin or oral sodium nitrite, they dilate both the systemic arterial and venous beds[15] (Fig. 4). In this manner, arterial blood pressure falls slightly and central venous pressure is reduced, resulting in peripheral venous pooling and a fall in stroke volume and cardiac output. In contrast, the rapid introduction of the nitrites into the circulation following inhalation of amyl nitrite or the intravenous administration of nitroglycerin, results in profound arteriolar dilation and thereby a marked fall in arterial blood pressure[15] (Fig. 4). Although present evidence indicates that changes in blood pressure in the physiologic range in man do not induce reflex alterations in venous tone, it is not unreasonable to anticipate that with marked reductions in pressure, such as occurs following inhaled amyl nitrite, baroreceptor stimulation results in reflex venoconstriction. Thus anti-adrenergic agents do not affect the mild venodilation produced by nitroglycerin, whereas they diminish the marked venoconstriction following amyl nitrite. Further, it is probable that the hyperventilation and anxiety which accompany the hypotension produced by amyl nitrite are responsible, in part, for the increase in adrenergic activity to the venous bed. The cardiac output is elevated as a consequence of the marked decline of the resistance to ventricular emptying coupled with the reflex constricting effect on the veins. In contrast, the decrease in blood pressure following the oral administration of the nitrites is less marked, and is not associated with increased respiration. Thus, reflex venoconstriction does not occur and the direct action of venodilation is observed. From these findings in intact man, it can be concluded that the principal direct action of sublingual nitroglycerin is on the veins and of inhaled amyl nitrite on the arterial bed.

NITRITES
Actions on the Peripheral Circulation

	Arterial pressure	Systemic vascular resistance	Venous tone	Cardiac output
Nitroglycerin sublingual	↓	↓⃝	↓⃝	↓
Nitroglycerin intravenous	⬇	⬇⃝	⬆	⬆
Amyl nitrite inhaled	⬇	⬇⃝	⬆	⬆
Sodium nitrite oral	↓	↓⃝	↓⃝	↓

↑ Small increase ⬆ Large increase
↓ Small decrease ⬇ Large decrease
◯ Direct action of nitrites

Figure 4. Actions of the nitrite drugs on circulatory dynamics.

The elucidation of these hemodynamic actions of the nitrites permits an understanding of the mechanisms by which these drugs relieve angina pectoris. Since angina pectoris may be viewed as an unfavorable relationship between myocardial oxygen demands and availability, the pain may be diminished by reducing the former and/or increasing the latter. This relationship may be improved by the vasodilator action of the nitrites on the coronary arteriolar bed to augment coronary blood flow and oxygen availability to the heart, or by the vasodilator action on the peripheral vascular bed to reduce the work the heart must perform to pump blood. These drugs clearly produce vasodilation of the normal coronary vascular bed. However, they do not regularly increase coronary blood flow in patients with coronary arterial disease but may augment the development of collateral arterial anastomoses around the area of a coronary occlusion. In spite of the fact that the nitrites may not increase blood flow to the ischemic portion of the myocardium in patients with coronary atherosclerosis, many of these patients experience relief of their anginal symptoms during treatment with these drugs.

The possibility therefore was considered that the therapeutic action of the nitrites was dependent, in part, upon their effects on the peripheral circulation (Fig. 4). Since sublingual nitroglycerin results in dilation of the systemic veins and peripheral pooling of blood, the drug diminishes indirectly the size of the heart. As mentioned previously, the oxygen requirements of the myocardium are directly related to the tension which the ventricle develops during systole. Since this tension is determined by the intraventricular systolic pressure and the volume of the ventricular cavity, a reduction of ventricular size diminishes the oxygen demand of the heart. Indeed, it has been shown that ventricular dimensions are reduced by nitroglycerin in man[16]. Since ventricular size is related to the development of myocardial tension and oxygen consumption, the reduction of ventricular size tends to reduce cardiac oxygen requirements and explains, at least in part, the salutary effects of sublingual nitroglycerin in providing relief from anginal pain. In addition, the fall in arterial resistance and reduction in arterial pressure produced by the nitrite diminish the resistance to ventricular ejection and reduces intraventricular pressure, thereby lowering myocardial oxygen consumption. Thus the vasodilator actions of nitrites on both the venous and arterial beds are importantly related to the improvement in the relationship between cardiac oxygen availability and demands by the reduction of myocardial oxygen consumption.

The efficacy of inhaled amyl nitrite in patients with angina pectoris is related to its predominant effect on the arterial bed of markedly reducing systemic vascular resistance. In this manner, resistance to ventricular emptying is diminished and myocardial oxygen consumption is lowered. Thus the tendency for reflex augmentation of venous return to increase the work of the heart is overridden by the more marked effect of the reduction of intraventricular systolic pressure to diminish myocardial oxygen demands.

Propranolol

In this section the mechanism of action and therapeutic applications of the beta-adrenergic receptor blocking drug, propranolol, are considered[17]. It is useful both from a clinical and pharmacologic standpoint to divide the end-organ receptors for the sympathetic nervous system into two basic types, alpha and beta-adrenergic receptors (Fig. 5). In regard to the cardiovascular system, only beta-receptors are located in the heart, while both alpha and beta-receptors are present in the peripheral vascular beds. Activation of the alpha-receptors results in arteriolar constriction, and stimulation of beta-receptors produces arteriolar dilation and augments cardiac contractility and increases the heart rate. Methoxamine is a pure alpha-adrenergic stimulating drug, isoproterenol a pure beta-adrenergic activating drug, while epinephrine and norepinephrine are combined alpha and beta-stimulating drugs. Importantly, there are a group of sympathomimetic drugs, of which metaraminol, amphetamine, and ephedrine are employed most frequently in clinical practice, that activate indirectly the sympathetic nervous system through the release of the sympathetic neurotransmitter, norepinephrine, from adrenergic nerve endings. Drugs capable of effecting alpha-adrenergic receptor blockade, such as phenoxybenzamine and phentolamine, have been available for some time. The recent introduction of propranolol has provided a means for the selective blockade of the cardiotonic and cardiac rate accelerator actions of sympathetic nerve stimulation and of the catecholamines-epinephrine, norepinephrine, and isoproterenol. Interestingly, in the arteriolar beds, humorally transported norepi-

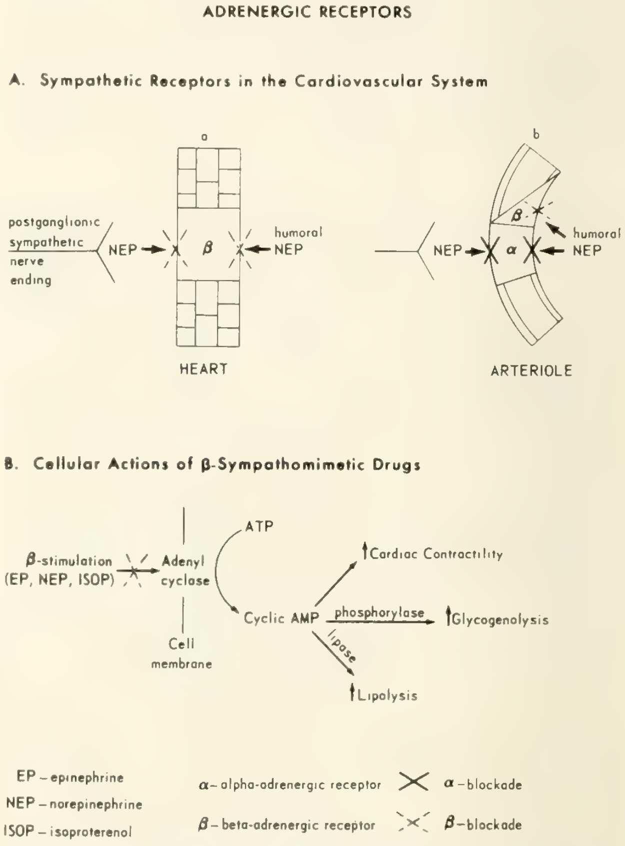

Figure 5. Diagrammatic representatives of (A) sympathetic receptors in (a) the heart and (b) the arteriolar bed, and (B) the cellular actions of beta-sympathomimetic drugs. A. While both neuronally released and humoral norepinephrine stimulate cardiac beta-receptors and arteriolar alpha-receptors only humoral norepinephrine activates arteriolar beta-receptors. B. Bet-adrenergic activity is initiated by stimulation of, and beta-adrenergic blocking action is exerted by the inhibition of the enzyme adenyl cyclase which, in turn, effects the formation of cyclic AMP (3', 5'-adenosinemonophosphate). Cyclic AMP then mediates a stimulating action on cardiac muscle and metabolic effects on carbohydrate and fat metabolism.

nephrine acts on both alpha and beta-receptors, while neuronally released norepinephrine stimulates only alpha-receptors. It should be remembered that the unique alpha and beta-adrenergic receptor blocking drugs are quite specific in their blocking actions at the end-organ. In contrast, antiadrenergic drugs such as reserpine and guanethidine which deplete the catecholamine stores of the sympathetic nerve endings of the body, decease both alpha and beta-adrenergic nervous system activity, while ganglionic blocking agents such as hexamethonium exert a combined inhibiting action on the entire sympathetic and parasympathetic nervous systems.

It is now though that the beta-adrenergic receptors are intimately related to the membrane enzyme adenyl cyclase which mediates the intracellular transformation of ATP to cyclic AMP (Fig. 5). Cyclic AMP, formed by the action of beta-adrenergic stimulating drugs on adenyl cyclase, apparently is the substance responsible for the augmentation of myocardial contractility. This cardiotonic action of cyclic AMP may be mediated by the effect of this substance on membrane permeability to increase the influx of calcium into the cell. In addition, cyclic AMP appears to regulate the metabolic effects of adrenergic stimuli on carbohydrate and fat synthesis. The substance activates phosphorylase to break down glycogen, resulting in an increase in blood glucose from the liver and an increase in blood lactate from muscle. Cylic AMP stimulates lipase to activate the lipolysis of triglycerides in adipose tissue to free fatty acids.

The therapeutic application of propranolol is now the subject of intensive clinical evaluation for conditions in which the intensity of sympathetic drive to the heart is potentially excessive. One of the most important clinical uses of propranolol has been in the treatment of patients with angina pectoris. By the prevention of the increase in myocardial oxygen requirements induced by the stimulation of the cardiac sympathetic nerves during exertion, the agent has proven to be of value in reducng anginal symptoms. Propranolol provides relief of angina pectoris by reducing myocardial oxygen consumption by lowering heart rate and arterial pressure, as well as by decreasing the velocity of contraction and the extent of systolic shortening of the ventricle.

Another important clinical application of propranolol is in the antagonism of certain cardiac arrhythmias. In this regard, the drug has been particularly successful in the treatment of digitalis-induced ventricular arrhythmias and non-digitalis related supraventricular arrhythmias. Beta-adrenergic blockade is effective in reducing the rapid ventricular rate in patients with atrial fibrillation and atrial flutter and this effect is additive to that exerted by digitalis. In the treatment of atrial fibrillation or flutter, propranolol usually has little effect on atrial rate, but its clinically beneficial effects result from a prolongation of the refractory period of the atrioventricular node and a consequent diminution in the number of supraventricular impulses which are conducted to the ventricles. Since the ventricular rate in supraventricular tachycardias can be rapidly brought under control by the intravenous administration of propranolol, this drug is effective in the acute management of these arrhythmias, particularly those provoked by digitalis. Further, since fatal arrhythmias can follow the use of electrical countershock in the presence of excessive or even normal amounts of digitalis, the use of propranolol is preferable to electrical conversion in patients with sustained supraventricular or ventricular tachycardias which might be related to digitalis.

The antiarrhythmic properties of propranolol are the result of two effects. One of these actions is related to beta-adrenergic blockade, since adrenergic stimuli increase ventricular automatically and predispose to the development of digitalis-induced arrhythmias. The other action is the result of a quinidine-like effect on cardiac muscle; the refractory period is prolonged and pacemaker activity is diminished by propranolol. It is postulated that arrhythmias related to excessive sympathetic activity are relieved by the antiadrenergic actions of propranolol and those not accompanied by high levels of adrenergic activity by the quinidine-like effects of the drug.

Summary

The mechanisms of action and therapeutic uses of digitalis, quinidine, nitroglycerin, and propranolol have been reviewed in order to provide the understanding required for a more rational use of these drugs in patients. Necessarily, this presentation has been brief and has included some speculative material without attempting to bring out all of the viewpoints in areas in which some controversy remains. The primary indication for the use of digitalis is the presence of heart failure secondary to absolute or relative myocardial dysfunction, regardless of the setting in which the decompensation occurs. Since the glycoside improves the contractile state of the non-failing heart, the drug provides a protective action on the myocardium in the face of unusual stresses on the cardiovascular system and thus its use may be helpful in special situations in some patients without heart failure.

Although quinidine exerts many potentially beneficial actions on the electrical activity of the heart for the inhibition of arrhythmias, its principal effect in this regard appears to be related to its ability to prolong the functional refractory period of cardiac muscle. With respect to nitroglycerin, it seems likely that the remarkable clinical effects of this drug in interrupting the pain of coronary ischemia is dependent on its actions on the peripheral circulation, particularly in patients in whom angina is relieved without an accompanying decrease in coronary vascular resistance, and is related to a combination of peripheral and coronary vasodilator effects in patients in whom the affected coronary vessels and available collateral channels are capable of response.

The principal clinical uses of propranolol are in the treatment of angina pectoris and cardiac arrhythmias. In regard to angina pectoris, the drug exerts its beneficial effect by reducing myocardial oxygen requirements, although propranolol interferes with the mechanical pumping action of the heart. Therefore, beta-adrenergic blocking drugs are most useful in patients whose exercise capacity is limited by an unfavorable relationship between myocardial oxygen requirements and availability, while they may be harmful to patients who are limited by myocardial failure.

At the cellular level, it was indicated that the drugs which act on the heart may do so by exerting certain effects on the cell membrane without necessarily entering the intracellular space. The positive contractile actions of digitalis, and the negative cardiotonic actions of quinidine and propranolol are thought to be ultimately related to the amount of calcium available to the contractile proteins. In addition, the arrhythmia-producing actions of digitalis and the antiarrhythmic properties of quinidine and propranolol are, to a major extent, a consequence of certain cellular fluxes of sodium and potassium. Although it is clear that the range of clinical applications of these cardiovascular drugs is being expanded, it is apparent that the proper use of these agents remains a matter of expert clinical judgment.

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Experience With External Cardiac Resuscitation In A Community Hospital

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The introduction of closed chest cardiac massage (1) and the development of external defibrillation (2-4) have considerably enhanced the possibility of successful cardiac resuscitation. Numerous series have been reported by University Hospitals (5-10), however, only a few series have originated in community hospitals (11 & 12). We propose to report on the experience with cardiopulmonary resuscitations outside of the operating theater in a 654 bed community hospital. In this study, cardiac arrest is defined as sudden and unexpected clinical death (5 & 13). Our series includes 142 patients and covers a two year period from 1/6/65 to 1/5/67. This represents the second largest single series in the literature utilizing external massage outside of the operating theater (5). Twenty-one patients were successfully resuscitated and 16 are still alive and well.

Methods

In our hospital we have adapted the principles and techniques of external cardiac massage, ventilation and defibrillation as formulated by the Johns Hopkins group and others (5, 14, & 15) and recently outlined by the National Academy of Sciences-National Research Council (16).

When a cardiac arrest occurred, a special number "1-2" was dialed, illuminating a red light on the switchboard; a code on the public address system indicated the site of the emergency. All medical house officers, an anesthesiologist, an inhalation therapist, a nursing supervisor, and an ECG technician proceeded to the site of "arrest". At night the same procedure was employed. A medical resident was required to be in the hospital at all times.

Emergency carts and D.C. defibrillators, strategically placed throughout the hospital, were brought to the specified site by designated personnel. The nursing staff, trained in resuscitative techniques, immediately instituted such therapy, and continued until a physician assumed responsibility.

Most of the patients were initially ventilated using either mouth to mouth breathing through an oral airway, or a face mask and Ambu bag. In 95% of the patients, subsequent ventilation was accomplished by means of a cuffed endotracheal tube and an Ambu bag using oxygen flows of 7 to 12 Liters per minute. Attempts were made to obtain arterial blood samples early in the course of resuscitation for pH, PO_2 and PCO_2. All analyses were performed at least twice using standard techniques.

A special staff committee supervised and coordinated the cardiac arrest program and the training of personnel. Pertinent data on each arrest were noted by the medical resident on a pecial form filed with the cardiac arrest committee. The patient's name, and the time and site of the emergency were recorded by the switchboard operator and noted by the nursing supervisor.

In all instances, the data presented are those of the patient's first arrest. One patient (T.R., Cases 94 & 113) had two arrests on two different admissions.

Post mortem examinations were performed in 68 (48% of our patients.)

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Results

During a two year period, 142 patients underwent cardio-pulmonary resuscitation at Saint Francis Hospital (65 in 1965 and 77 in 1966); 83 were males and 59 were females. Two-thirds were 60 years old or over with a mean age of 63.5 (Table #1). Eighty-two patients had ventricular fibrillation, 56 standstill, and in four, the type of arrest was unknown. Table #2 summarizes the primary diagnosis. Acute myocardial infarction was the leading cause of arrest.

Forty-five patients (32%) were restored to their pre-arrest cardiac and central nervous system status. Of this group, 21 patients (15% of the total series) were long-term survivors: 20 were ultimately discharged from the hospital and one patient (Case #125), ready for discharge, died of an acute myocardial infarction nineteen days after successful resussitation. Eighteen of our patients had pulmonary embolism (proven at autopsy in 16) and four had myocardial infarction with myocardial rupture; if these 22 patients were excluded because successful restoration of circulation was mechanically impossible, our series would have shown 38% successful resuscitations, including 18% long-term survivors. Seventeen additional patients included in this series were considered to be unsalvagable.

Table #3 demonstrates that the best long-term survival rate was obtained in the Cardiac Laboratory (100%) followed by the Emergency Room (56%), the Coronary Care Unit (13%), the Intensive Care Unit (9% and finally the General Wards (6%).

TABLE 1

AGE DISTRIBUTION OF 142 CASES AND RESULTS

Age (Years)			30-39	40-49	50-59	60-69	70-79	80 and over
No. of cases		(142)	6	11	31	44	41	9
Pre-arrest status restored	Short-term survivors	(24)	2 (33%)	—	10 (32%)	6 (14%)	4 (10%)	2 (22%)
	Long-term survivors*	(21)	2 (33%)	2 (18%)	6 (19%)	5 (11%)	4 (10%)	2 (22%)
	Total	(45)	4 (66%)	2 (18%)	16 (51%)	11 (25%)	8 (20%)	4 (44%)

* All of the Long-term survivors except one patient (case #125) were discharged from the hospital (see text)

TABLE 2

UNDERLYING DISEASES WITH RESULTS

Disease	No. of Patients	Pre-Arrest Status Restored			
		Short-term survivors		Long-term survivors	
Acute Myocardial Infarction	70	12	(17%)	10	(14%)
Coronary Heart Disease with Failure	10	2	(20%)	1	(10%)
Coronary Heart Disease without Failure	19	2	(11%)	3	(16%)
Acute Pulmonary embolism	18	1	(6%)	0	
Others	25	7	(28%)	7	(28%)
Total	142	24	(17%)	21	(15%)

TABLE 3

SITE AND OUTCOME OF ARREST IN ALL CASES

Site	No. of Patients	Pre-Arrest Status Restored					
		Short-term survivors		Long-term survivors		Total	
Cardiac Lab	3	0		3	(100%)	3	(100%)
Emergency Room	9	0		5	(56%)	5	(56%)
Coronary Care Unit	45	9	(20%)	6	(13%)	15	(33%)
Intensive Care Unit	33	11	(33%)	3	(9%)	14	(42%)
Ward	51	4	(8%)	3	(6%)	7	(14%)
Hospital Corridor	1	0		1		1	(100%)
Total	142	24	(17%)	21	(15%)	45	(32%)

The time of arrest is shown in Table #4. It is evident that the poorest results were obtained at night. The mean resuscitation time was 48 minutes in the 97 unsuccessful cases, 33 minutes in the 24 short-term survivors restored to their pre-arrest status, and 11 minutes in the 21 long-term survivors.

Data on the 21 survivors are summarized in Table #5. The mean age was 61 years. Sixteen patients are still alive with a survival time of 20-23 months in three, 15-16 months in six, four to six months in four, and one to two months in three. Ventricular fibrillation was the mechanism of arrest in 18 patients and standstill in three. Twenty-two percent of patients with ventricular fibrillation were long-term survivors versus 5% of those with standstill. Table #1 indicates that the rate of success was definitely higher in the younger age group, however, 22% of patients over age 80 were long-term survivors.

Table #6 shows the survival time in 97 patients who could not be restored to their pre-arrest central nervous system status: 55% of this group expired within one hour after cardiac arrest and 88% within one day. Only 3% survived more than one week.

Analysis of patients with acute myocardial infarction, including those in heart failure and cardiogenic shock, reveals an overall long-term survival rate of 14%. Thirty four patients had their arrest in the Coronary Care Unit and six survived (18%). Only one of 29 patients who had their arrest in the wards or in the intensive care unit survived (3%).

The complications of external massage in 31 autospied patients were as follows: Twenty-eight patients with rib fractures, 16 with sternal fractures, two with lacerations of the liver, four with lacerations of the spleen, and one with a pneumothorax.

A total of 159 aterial blood samples obtained during 54 resuscitations procedures on 51 patients were analyzed for pH, PO_2 and PCO_2. Of these, 50 were obtained during the first thirty minutes after the onset of cardiac arrest and will be discussed because they proved most valuable in guiding therapy and evaluating resuscitative efforts. Almost all patients had received 90 meg. of sodium bicarbonate intravenously during the initial five minutes of resuscitation.

Wide variations were noted in arterial blood pH and gas tensions (Table #7). Both inadvertent underventilation and overventilation were common, and on occasion documented in a given patient at different times. Significant acidosis was noted on initial blood analysis in 29 of 54 cardiac arrests (54%). In 22, the arterial pH was below 7.30 with a range of 6.93 to 7.27. In 66% of the patients with acidosis, there was an elevated PCO_2 (45.5—106 mm. Hg.) indicating that acidosis was at least in part respiratory origin.

Inadvertent overventilation leading to significant hypocapnia and alkalosis was initially present in eight patients with a pH greater than 7.47 and a PCO_2 below 31 mm. Hg.

The following illustrative cases are briefly reported:

Case Reports

S.K. Case 8. This 60-year-old white male was admitted with a chief complaint of chest pain of 24 hours duration. There was no evidence of cardiac failure or shock. The initial electrocardiogram revealed an acute antero-septal myocardial infarction. Shortly after admission, the patient developed ventricular fibrillation. Regular sinus rhythm was restored within one minute with closed chest massage and ventilation by an Ambu bag without recourse to defibrillation. He was discharged four weeks later and is well at the time of this report.

T.R. Case 94 & 113. This 72-year-old white male, with a past history of myocardial infarction and congestive heart failure, was admitted for exodontia on 4/17/66. He later developed chest pain and diaphoresis. On 4/18/66, the patient developed ventricular fibrillation and was successfully resuscitated. Subsequent electrocardiograms were not diagnostic of an acute process. For the next two weeks, the patient had confusion followed by complete amnesia for the events during this period. He was alert on discharge 5/13/66. On 6/13/66, he re-entered with the chief complaint of sudden

Table 4

Time of Arrest and Results

Hour			7:00 A.M.—3:00 P.M.	3:00 P.M.—11:00 P.M.	11:00 P.M.–7:00 A.M.
No. of Cases		(142)	60	43	39
Pre-arrest status restored	Shot-term survivors	(24)	9 (15%)	10 (23%)	5 (13%)
	Long-term survivors	(21)	10 (17%)	7 (16%)	4 (10%)
	Totals	(45)	19 (32%)	17 (39%)	9 (23%)

TABLE 5

DETAILS OF 21 SURVIVORS

Patient & Case #	Sex	Age	Location*	Date of Arrest	Diagnosis at time of Arrest	Resuscitation time (min.)	Type of Arrests**	Comments and Follow-up
S.K. 8	M	60	CCU	3/7/65	Acute Myocardial infarction	1	V.F.	Spontaneous defibrillation Still Alive (See Case Report)
R.N. 18	M	36	CL	4/30/65	Chest pain of unknown etiology. Normal coronary arteriogram.	< 1	V.F.	Arrest during selective coronary arteriography. Still alive
A.B. 28	F	43	CL	6/28/65	Chest pain of unknown etiology. Normal coronary arteriogram.	< 1	V.F.	Arrest during selective coronary arteriography. Still alive
H.M. 43	F	65	Ward	10/1/65	Metastatic carcinoma of head of pancreas	10	V.S.	Arrest 1 day after laporotomy. Dis. 10/16/65 Exp. 12/5/65
J.F. 44	F	53	Ward	10/3/65	Rheumatoid arthritis Drug reaction	30	V.F.	Arrest 15 min. after injection of nalorphine to counteract respiratory depression due to meperidine. Still alive
J.S. 45	M	82	ER	10/8/65	Lacerated scalp Severed artery	2	V.S.	Bled profusely from occipital artery. Still alive
J.S. 54	M	55	hospital corridor	10/28/65	Probable acute myocardial infarction	20	V.F.	Discharged 11/26/65 Expired 12/5/65
L.B. 55	M	51	CCU	11/1/65	Acute myocardial infarction	30	V.F.	Still alive
J.B. 57	M	49	CL	11/23/65	Coronary heart disease	< 1	V.F.	Arrest during selective coronary arteriography. Still alive
T.S. 69	M	71	ER	1/10/66	Probable acute myocardial infarction	25	V.F.	Still alive
J.B. 74	F	35	Ward	1/28/66	Ulcerative colitis Post-op colectomy	30	V.F.	Volume depletion and electrolyte imbalance. Still alive

T.R. 94	M	72	CCU	4/18/66	Probable acute myocardial infarction	5	V.F.	1st Admission See Case Report
T.R. 113	M	72	ER	6/15/66	Acute myocardial infarction	30	V.F.	2nd Admission. See Case Report. Expired 7/27/66
A.M. 118	M	61	ICU	8/4/66	Acute myocardial infarction	10	V.F.	Still alive
J.R. 124	M	88	CCU	8/26/66	Acute myocardial infarction. Heart block.	3	V.F.	Subsequent insertion of permanent transvenous pacemaker. Still alive
G.C. 125	F	59	ICU	9/8/66	Coronary heart disease Post Vineberg procedure	4	V.F.	Died of acute myocardial infarction 9/27/66
P.K. 131	M	66	ER	10/3/66	Coronary heart disease Pulmonary edema	16	V.F.	? digitalis toxicity Still alive
A.G. 135	M	59	CCU	10/25/66	Acute myocardial infarction. Heart block, transient.	1	V.S.	Still alive Normal sinus rhythm
S.S. 140	F	73	ICU	12/10/66	Complete heart block	3	V.F.	Subsequent insertion of permanent transvenous pacemaker. Still alive
L.S. 141	M	68	ER	12/10/66	Coronary heart disease Alcoholism	5	V.F.	Still alive
H.C. 142	M	54	CCU	1/5/67	Acute myocardial infarction	4	V.F.	Heart block treated with temporary venous pacemaker, 1/6/67. Disch. 2/5/67. Still alive. See Case report

* CCU—Coronary Care Unit
CL—Cardiac Laboratory
ICU—Intensive Care Unit
ER—Emergency Room

** V.F.—Ventricular fibrillation
V.S.—Ventricular standstill

Table 6

Survival Time

Time	Short-term survivors restored to pre-arrest status	Failures
One hour or less	2	53
1-3 hours	7	25
3-7 hours	1	6
7-15 hours		1
1-3 days	7	1
3-5 days	4	5
5-7 days		3
1-5 weeks	3 (8,10,21,days)	3 (7,10,31,days)
Total	24	97

severe chest pain and shortness of breath. The electrocardiogram showed rapid ventricular tachycardia, which on lead V_5 changed to ventricular fibrillation (Fig. 1). Cardiac resuscitation was instituted and he was successfully defibrillated. Serial electrocardiograms revealed the evolution of a recent posterior myocardial infarction. He was disoriented for a period of several days and thereafter had amnesia for the whole period. He was discharged on 7/19/66 in satisfactory condition, but he expired at home one week later.

H.C. Case 142. This 54-year-old white male was admitted with acute anteroseptal myocardial infarction on 1/5/67. At 7:30 A.M. shortly after admission to the coronary care unit, he developed ventricular fibrillation. External cardiac massage and artificial ventilation were maintained by the nursing staff for four minutes as evidenced by a continuous electrocardiographic recording. He was successfully converted with direct current shock on the arrival of a resident physician (Fig. 2). On the following day, heart block supervened and a temporary transvenous pacemaker was inserted. Subsequently, the patient reverted to normal sinus rhythm and the pacemaker was removed. He was discharged on 2/4/67 in satisfactory condition.

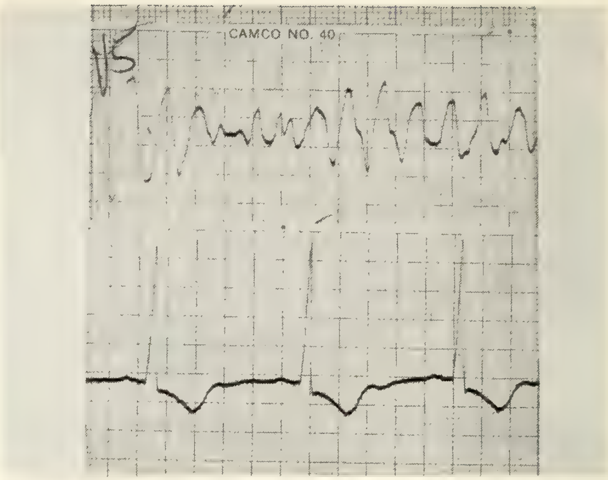

Figure 1 (Case 113). Ventricular fibrillation converted to normal sinus rhythm (Lead V_5).

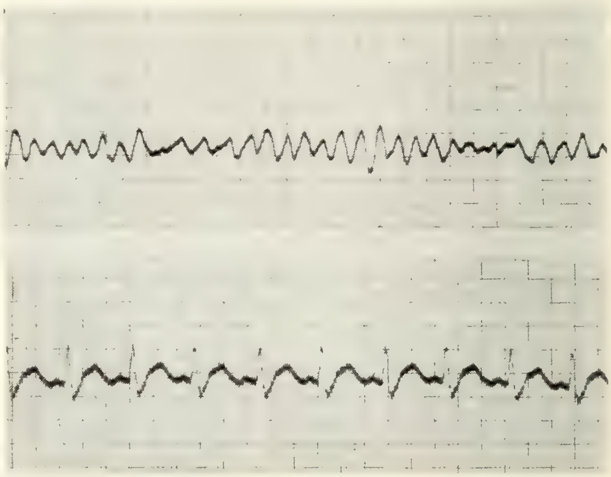

Figure 2 (Case 142). Strip of a four minute run of ventricular fibrillation during massage by nursing staff. Successful defibrillation.

Table 7

Arterial Blood Gas Tensions and pH During First 30 Minutes

	Patient Category		pH	PO_2 mm. Hg.	PCO_2 mm. Mg.
Restored to pre-arrest CNS status	Long-Term Survivors (4 Patients)	Mean	7.45	96	32.5
		Range	7.38-7.52	51-152	18-47
	Survivors Short-Term (8 Patients)	Mean	7.39	116	47.6
		Range	7.06-7.56	38-295	21-90*
Not restored to pre-arrest CNS status	Survivors for more than 1 day (8 Patients)	Mean	7.27	137	41.4
		Range	7.07-7.55	36-265	21-63
	Total Failures (30 Patients)	Mean	7.29	56	54.1
		Range	6.93-7.56	7-150**	21-110***

* Only 2 patients out of 8 had a PCO_2 above 47 mm. Hg.

** 6 patients had an initial PO_2 of 16 mm. Hg. or less

*** 15 of the 30 patients (50%) had a PCO_2 of 50 mm. Hg. or more

R.N. Case 27. This 75-year-old white male was admitted to the hospital on 6/24/65 with a complaint of black stools, dyspnea and ankle edema. Shortly after admission, he went into ventricular fibrillation, received external massage, was intubated, and successfully defibrillated. Within minutes he was awake. He tolerated the endotracheal tube so poorly that two hours after cardiac arrest, it was elected to withdraw the tube; following its removal, there was no evidence of laryngospasm or aspiration. However within minutes he became cyanotic and subsequently ventricular fibrillation recurred. An endotracheal tube was reinserted with some difficulty and resuscitation efforts resumed without results. He expired two hours and fourteen minutes after his initial cardiac arrest. Removal of the airway was considered a key factor in his sudden leterioration after an excellent initial result.

Discussion

We have reported on the results of our cardiac arrest program supervised by a staff committee and executed by a team of physicians, well trained nurses, and inhalation therapists in a community hospital. In a two year period, 45 patients were successfully resuscitated had 20 of these were discharged from the hospital in satisfactory mental and physical condition. Our report underlines the successful application of external cardiac massage in areas of the hospital where in the past only an occasional resuscitation was possible.

Our study indicates that the rate of success of resuscitative techniques in a community hospital can compare favorably with those published by University hospitals. Long-term survivors represented 15% of our series.

In Jude's series (5) of 224 patients compiled during a five year period outside the operating theater, 16% were long-term survivors. Inordinately high survival rates have been reported in some small series reviewed by Jude et al (5). Moreover, the survival rate in many reports has been inflated by the inclusion of arrests in the operating room (13). In those large series excluding cardiac arrest in the operating theater, the percentage of survivors has ranged from 5-6% (9, 10 & 17) to 14% (6 & 7).

Our study revealed that the success rate was highest in areas of the hospital where cardiac arrest could be recognized immediately by monitoring, and resuscitative techniques could be applied without delay (Cardiac Laboratory, Emergency Room, and Coronary Care Unit).

Successful resuscitation was relatively infrequent at night (Table 4). Several factors may explain this finding: relative shortage of nurses, lack of immediate detection, and a reduced number of house physicians.

A sense of urgency in initiating resuscitation is a prerequisite for a successful outcome. In our series, the role of the nurses in starting resuscitative measures was essential, as evidenced by one of our survivors (Case 142) in whom nurses carried out external massage and ventilation for the initial four minutes.

Our successful experience with defibrillation in the cardiac laboratory without resortaing to massage or ventilation illustrates the efficacy of this approach when cardiac arrest and its mechanism can be detected immediately. Immediate defibrillation might restore normal circulation without delay, "save the heart from irreparable damage" (18), and would avoid the complications of massage. We feel that well trained nurses in the Emergency Room, Coronary and Intensive Care Units should be permitted to use a defibrillator, and this policy has been recently adopted in our hospital.

There should be no delay in alerting the cardiac arrest team: In our hospital, dialing "1-2" evokes an immediate response from the telephone operator and a special call on the public address system. To ensure that a physician will be available, medical house officers are instructed to proceed immediately to the designated floor; thereafter, only the required complement remains.

The anesthesiologist should not leave the area of the emergency until he has inserted an endotracheal tube and established adequate ventilation, which can be maintained by the inhalation therapist under supervision. The premature removal of the endotracheal tube in three of our patients who were successfully resuscitated, but tolerated the tube poorly, resulted in rapid deterioration and death (Case 27). Such patients are now being sedated and ventilated by mechanical respirators for several hours; the endotracheal catheter is removed only when the stability of the patient is established and in the presence of an anesthesiologist, should immediate reintubation be necessary. It is now our policy to have all endotracheal tubes removed by anesthesiologists.

Our series demonstrates that the shorter the period of resuscitative effort the higher is the rate of success: in two-thirds of the long-term survivors, the resuscitation time was ten minutes or less and none required more than one-half hour of massage. Prolonged efforts are occasionally rewarded by success, but such cases are exceptional (18).

In our experience, arterial blood pH and gas analysis have proved very helpful in the regulation of ventilation and administration of intravenous buffer solutions. Acidosis was found in 54% and alkalosis in 16% of the 51 patients studied. Carbon dioxide retention was a factor in 66% of the acidotic patients and hypoxemia was frequently encountered despite apparently adequate ventilation through an endotracheal tube. Our patients were deliberately hyperventilated when CO_2 retention was present, and in the presence of pure metabolic acidosis, when heart failure limited the use of sodium bicarbonate.

In one of our patients wth myocardial infarction (Case 8), ventricular fibrillation reverted spontaneously to normal sinus rhythm within one minute of external massage and ventilation: A handful of cases demonstrating this phenomenon have been reported (5 & 19).

Eighty-eight percent of the group that failed to respond to cardiopulmonary resuscitation expired within 24 hours (Table 6). Only three patients with irreversible cerebral damage survived for more than one week. This was a source of regret, but to quote Klassen et al (6) "is a relatively small price to pay when balanced against the excellent function obtained" in our successful cases.

The complications of external massage may be significant (5). Our complications proven by autopsy in 68 patients are generally similar to those reported in the literature (5 & 17). In the management of cardiac arrest, "it is especially important to realize that the worst complication—death—occurs with no treatment" (5).

Indexing terms: Arrest, Massage, Resuscitation.

Summary

A series of 142 cardiac arrests during a two year period in a community hospital has been presented and analyzed. Forty-five patients (32%) were restored to their pre-arrest cardiac and cerebral status, and of these, 21 (15%) were long-term survivors. The results compare favorably with those of similar large series reported by university hospitals.

This study emphasizes the need for swift recognition of cardiac arrest followed by immediate cardiopulmonary resuscitative measures administered by a well trained and well equipped team of physicians, nurses, technicians, and inhalation therapists. Arterial blood pH and gas studies were helpful during resuscitation.

Acknowledgments

We are indebted to Sister Mary Clare, Marie Aschenbrenner, L.P.N., Rosemary Solomson, L.P.N., Dorothea E. Bartlett and Dennis Rettinger for their assistance.

From 1/5/67 to 2/19/68, 26 additional patients were successfully resuscitated and discharged from our hospital in satisfactory condition.

This study was supported in part by a grant from the Heart Association of Greater Hartford, Inc.

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Automated Electrocardiography At A Community Hospital Utilizing Computer Diagnosis

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Introduction

Since May, 1965 Hartford Hospital has engaged in a demonstration project introducing automated processing and analysis of electrocardiograms in its Outpatient Department and Emergency Room Services.

This report describes the system employed.

Background

The number of diagnostic ECGs currently interpreted in hospitals, clinics, and health agencies presents a significant burden on physician time. The time required for reading and processing places a practical limitation on the number of ECG tracings that can be handled in a given institution. As a result, ECGs are usually ordered only when the physician sees a clear clinical indication for the test. If ECGs are to be employed for screening large numbers of apparently well people, automated rapid methods must be developed to handle the increased load.

Other reasons for developing automated techniques are the anticipated population increase without parallel increase in professional personnel, and the expanded number of beds planned for many community hospitals. These factors will result in an increased demand for diagnostic ECGs.

Much of a physicians work in reading ECGs is repetitious and tedious and can be performed by an electronic computer. A computer system has been developed by the Medical Systems Development Laboratory of the United States Public Health Service which can analyze ECGs without human intervention.[1,2,3] The computer system recognizes and identifies waveforms present on the traditional 12-lead tracing and correlates this information to synthesize an electrocardiographic diagnosis. Hartford Hospital has utilized the facilities of the Medical Systems Development Laboratory computer center to obtain machine reports on all of the ECGs taken on ambulatory patients in the Outpatient Department.

Method

Electrocardiograms are recorded on special data acquisition carts which simultaneously record the usual paper graphic tracing of the ECG and inscribe the signal on FM magnetic tape. (Figure 1) The machine provides dials for coding the patient's hospital chart number, the clinic or hospital of origin, the patient's height, weight, age, sex, race, blood pressure, whether or not the patient is on digitalis, quinidine or other drugs, and the ECG lead number. This information appears on the magnetic tape and on the paper graphic record. The ECGs are processed by an electronic computer located 340 miles away at the Medical Systems Development Laboratory in Washington, D.C. Access to the remote computer is accomplished by sending ECG signals over ordinary telephone wires to the computer center. A list of equipment utilized in this system is shown in Table 1. The signal may be sent directly to Washington as it is recorded from the patient. However, our usual method is to record and store ECGs on magnetic tape. When a full tape has been recorded (approximately 20 patients) the tape is played back with the output of the tape deck connected by cable to a Bell System

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This work was supported in part by Public Health Service Community Health Projects Grants Number CH-07-13-A65 and CH-07-13-B66, and by the Medical Systems Development Laboratory, Heart Disease Control Program, National Center For Chronic Disease Control.

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data-phone. When the technician lifts the receiver of the data-phone connecting the hospital with the computer center in Washington, tape recording equipment in Washington is activated. The stored ECGs are sent over the phone lines and re-recorded in Washington.

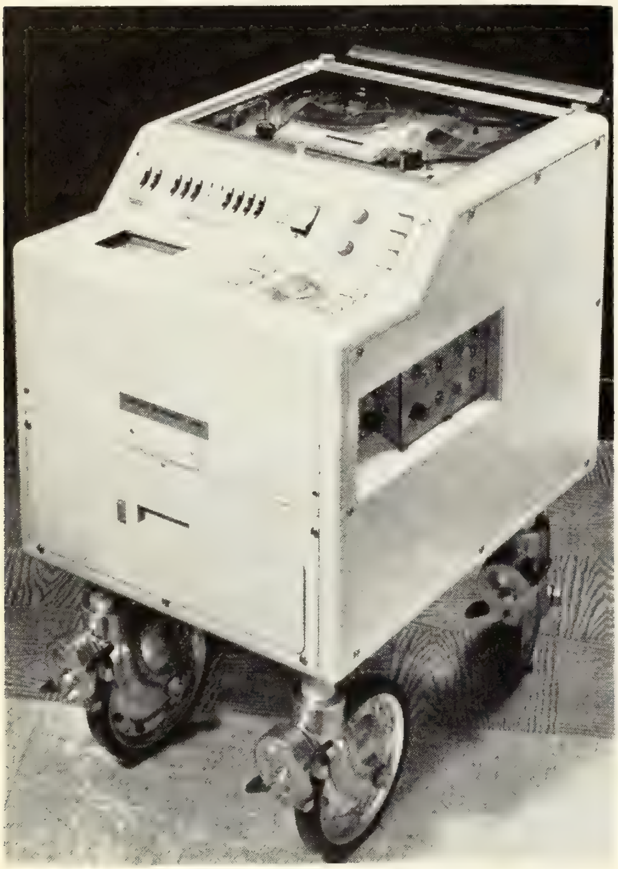


Figure 1
Data acquisition cart for recording ECGs on magnetic tape.

The voltage output of the ECG machine is ±2½ V. Resistors reduce this to ±2 V. for input into the data-phone. ECG information is primarily contained in the D.C. to 50 c.p.s. Hertz (Hz) band. This signal band is sent on the telephone lines by frequency modulation on a carrier frequency of 1988 c.p.s. in the voice range with an available band width of ±262 c.p.s. Thus the ECG signal is transmitted over the phone lines and can be monitored as an audible signal of varing pitch.

In Washington the tape recording of the received signal is placed on a unique input console and played again. The console demodulates the ECG signal from its carrier frequency and displays the ECG on an oscilloscope. A calibration signal sent from Hartford is observed and adjusted, to 1 cm. equals 1mV. The remainder of the processing is without human intervention.

The signal passes to an analogue-to-digital converter which samples the ECG 500 times a second and enters into the memory of a digital computer 500 numerical values/sec. representing the instantaneous voltage of the ECG every 2 milliseconds. The computer is a Control Data Corporation 160-A computer with additional core memory units and external computer tape storage. It has been programmed to accomplish several tasks.

First, the binary coded decimal information which precedes each lead of the ECG is decoded. This decoded message provides the patient identification characteristics entered by the Hartford technician. The message is stored on computer tape until it is printed in the final report. (Figure 2, top)

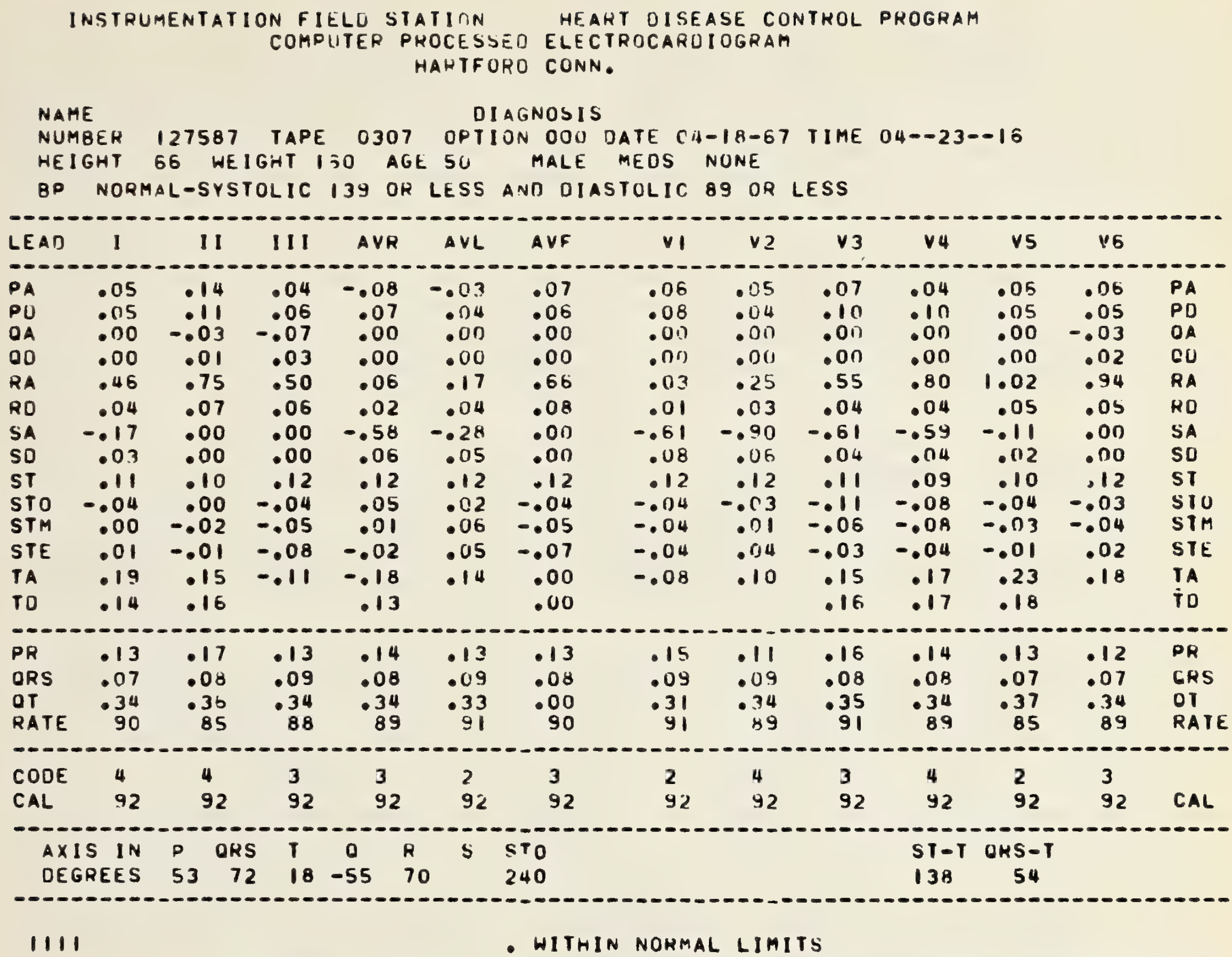
Second, in each lead the digitized ECG signal is examined and all waveforms present are identified and the height (amplitude in millivolts) and width (duration in seconds) measured. Measurements are made of the P P'QRST waves, the wave to wave intervals (R-R, P-R, QT) interwave segments (ST) and QRS duration. All 12 leads are measured sequentially and the results stored on the computer tape arranged as a table. (Figure 2)

Finally the computer program examines this table, compares the measurements in all leads with a predetermined set of criteria for normal values, and arrives at a diagnostic classification which is printed as a set of English language statements at the bottom of the report.[4] (Figure 2, bottom) The complete report is printed on a high speed printer. It contains all three categories of information:

1. Patient identification and characteristics
2. ECG lead measurements
3. Diagnosis

The reports are mailed to the Hartford Hospital Outpatient Department daily and are received 36 hours after being initially recorded. Over 5000 ECGs have been processed by this system in the past 1½ years.

The reports are utilized by project physicians in the daily reading of Outpatient Department ECGs. A physician simultaneously reviews the original ECG and the computer report. The computer report serves as the opinion of a "consulting cardiologist". It is highly accurate, but the project physician may disagree with the substance or completeness of the report in 10-15% of tracings.[5] When he agrees he merely initials the report. If he wishes to amend the report; he adds his comments at the bottom. The pertinent measurements and final ECG diagnosis are retyped on the sheet containing the mounted ECG. Both the mounted ECG



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    INSTRUMENTATION FIELD STATION     HEART DISEASE CONTROL PROGRAM
                  COMPUTER PROCESSED ELECTROCARDIOGRAM
                             HARTFORD CONN.

  NAME                                DIAGNOSIS
  NUMBER  127587  TAPE  0307  OPTION 000 DATE 04-18-67 TIME 04--23--16
  HEIGHT  66  WEIGHT 150  AGE 50    MALE  MEDS  NONE
  BP  NORMAL-SYSTOLIC 139 OR LESS AND DIASTOLIC 89 OR LESS
------------------------------------------------------------------------------------
LEAD    I      II     III    AVR    AVL    AVF       V1     V2     V3     V4     V5     V6
------------------------------------------------------------------------------------
PA     .05    .14    .04   -.08   -.03    .07       .06    .05    .07    .04    .05    .06    PA
PD     .05    .11    .06    .07    .04    .06       .08    .04    .10    .10    .05    .05    PD
QA     .00   -.03   -.07    .00    .00    .00       .00    .00    .00    .00    .00   -.03    QA
QD     .00    .01    .03    .00    .00    .00       .00    .00    .00    .00    .00    .02    QD
RA     .46    .75    .50    .06    .17    .66       .03    .25    .55    .80   1.02    .94    RA
RD     .04    .07    .06    .02    .04    .08       .01    .03    .04    .04    .05    .05    RD
SA    -.17    .00    .00   -.58   -.28    .00      -.61   -.90   -.61   -.59   -.11    .00    SA
SD     .03    .00    .00    .06    .05    .00       .08    .06    .04    .04    .02    .00    SD
ST     .11    .10    .12    .12    .12    .12       .12    .12    .11    .09    .10    ,12    ST
STO   -.04    .00   -.04    .05    .02   -.04      -.04   -.03   -.11   -.08   -.04   -.03    STO
STM    .00   -.02   -.05    .01    .06   -.05      -.04    .01   -.06   -.08   -.03   -.04    STM
STE    .01   -.01   -.08   -.02    .05   -.07      -.04    .04   -.03   -.04   -.01    .02    STE
TA     .19    .15   -.11   -.18    .14    .00      -.08    .10    .15    .17    .23    .18    TA
TD     .14    .16           .13           .00                     .16    .17    .18           TD
------------------------------------------------------------------------------------
PR     .13    .17    .13    .14    .13    .13       .15    .11    .16    .14    .13    .12    PR
QRS    .07    .08    .09    .08    .09    .08       .09    .09    .08    .08    .07    .07    QRS
QT     .34    .36    .34    .34    .33    .00       .31    .34    .35    .34    .37    .34    QT
RATE    90     85     88     89     91     90        91     89     91     89     85     89    RATE
------------------------------------------------------------------------------------
CODE    4      4      3      3      2      3         2      4      3      4      2      3
CAL     92     92     92     92     92     92        92     92     92     92     92     92    CAL
------------------------------------------------------------------------------------
  AXIS IN   P  QRS   T    Q    R    S   STO                        ST-T QRS-T
  DEGREES  53   72  18  -55   70        240                        138    54
------------------------------------------------------------------------------------

 1111                             . WITHIN NORMAL LIMITS
```

FIGURE 2

Complete computer report providing patient identification and characteristics followed by ECG lead measurements and ECG diagnosis. Wave measurements are presented as a column of figures for each of the twelve leads. Each wave is identified in the left hand column. An entry is made both for amplitude (A) in millivolts and duration (D) in seconds of each wave.

and the computer report are returned to the patient's chart.

Since September, 1966 a number of requisitioned electrocardiograms on Emergency Room patients have been taken on our magnetic tape data acquisition carts. Immediately after recording, the tape is played into the data-phone. The signal can be processed directly by the computer system. This eliminates re-recording and off-line processing which is unsatisfactory for Emergency Room reporting. The computer report is teletyped to Hartford Hospital. The report can be available in less than ten minutes from original recording. Figure 3 summarizes the various modes of transmission of ECG data employed in the Hartford Hospital project. At present, the rate limiting part of the system is the four minutes it takes to record a 12-lead ECG. It takes four minutes to send a single ECG over the phone lines. If the original is re-recorded at the computer center, it takes an additional four minutes to play back the signal into the computer console; compu-

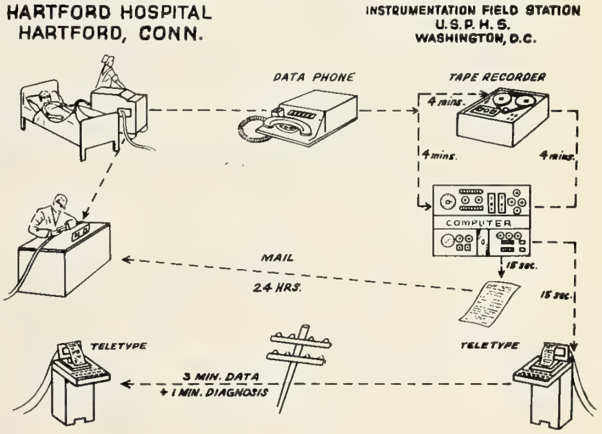


FIGURE 3

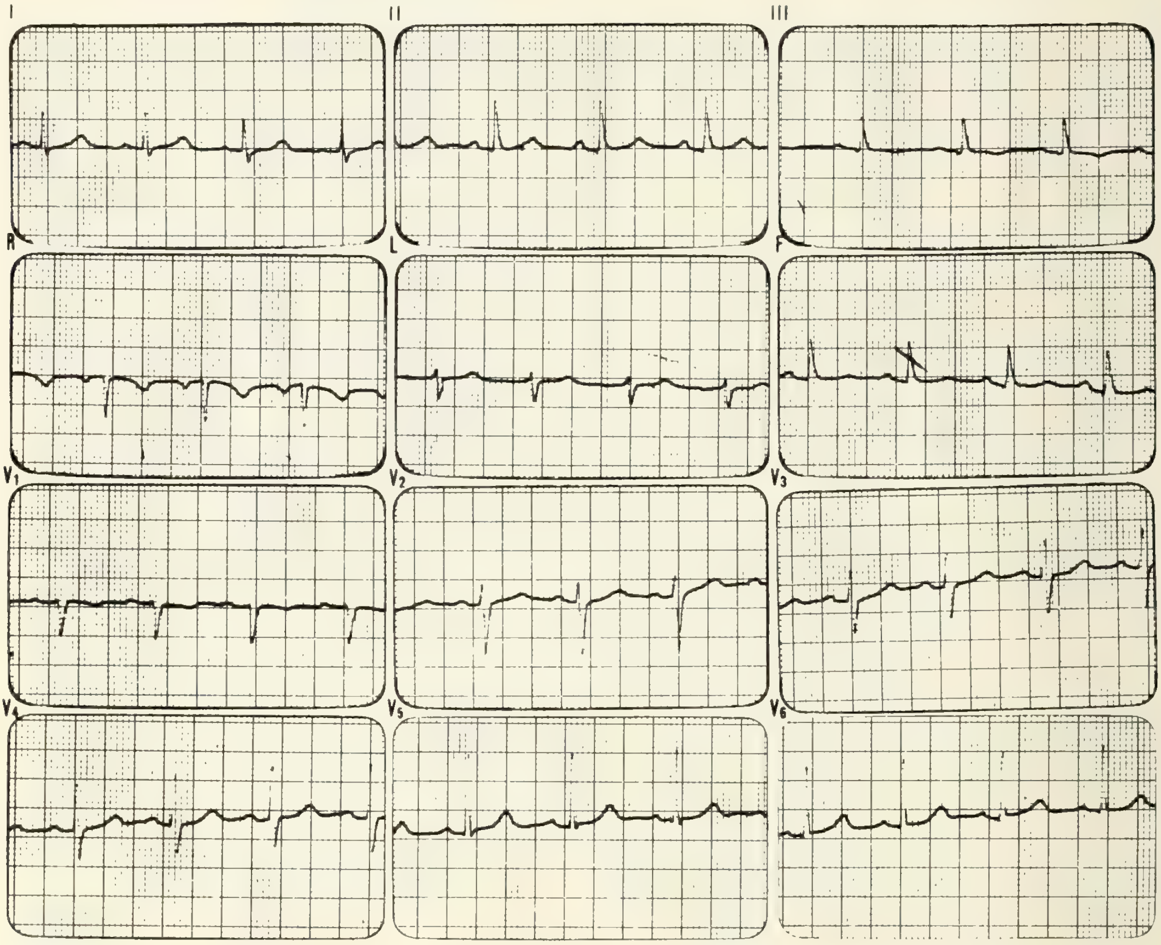
Modes of transmission of ECG data for remote computer processing and return of reports for use by Hartford Hospital physicians.

tation on each lead is completed in a few seconds. Once all twelve leads have been measured, the diagnostic program determines and prints its answers in only fifteen seconds. Teletyping a full report takes three to four minutes. As abbreviated report giving only the diagnosis and a few measurements can be sent in forty seconds.

Computer Diagnosis

The computer diagnostic program provides more than 110 individual ECG diagnoses and hundreds of combination statements. Terminology is familiar to all physicians. Standard text books and personal experiences were utilized in initially preparing the criteria, but criteria have been modified by project physicians in Washington on the basis of results of computer processing of over 50,000 ECGs. Information supplied to the Medical Systems Development Laboratory by Hartford Hospital on its clinical experience in reviewing computer read ECGs has resulted in changes in criteria and terminology making computer reports increasing acceptable as an aid to clinical ECG interpretation in this institution.

Examples of computer diagnosis of Hartford Hospital ECGs are presented:



HARTFORD HOSPITAL
DEPARTMENT OF MEDICINE EKG SCREENING PROJECT

NAME 7587	AGE 50	LOCATION	HOSPITAL NUMBER	DATE 4-18-67
PR .17	QRS .08	QT .34	RATE & RHYTHM 85	MEAN QRS AXIS 72°
DESCRIPTION	Within normal limits			

FIGURE 4
Normal ECG with abbreviated computer interpretation.

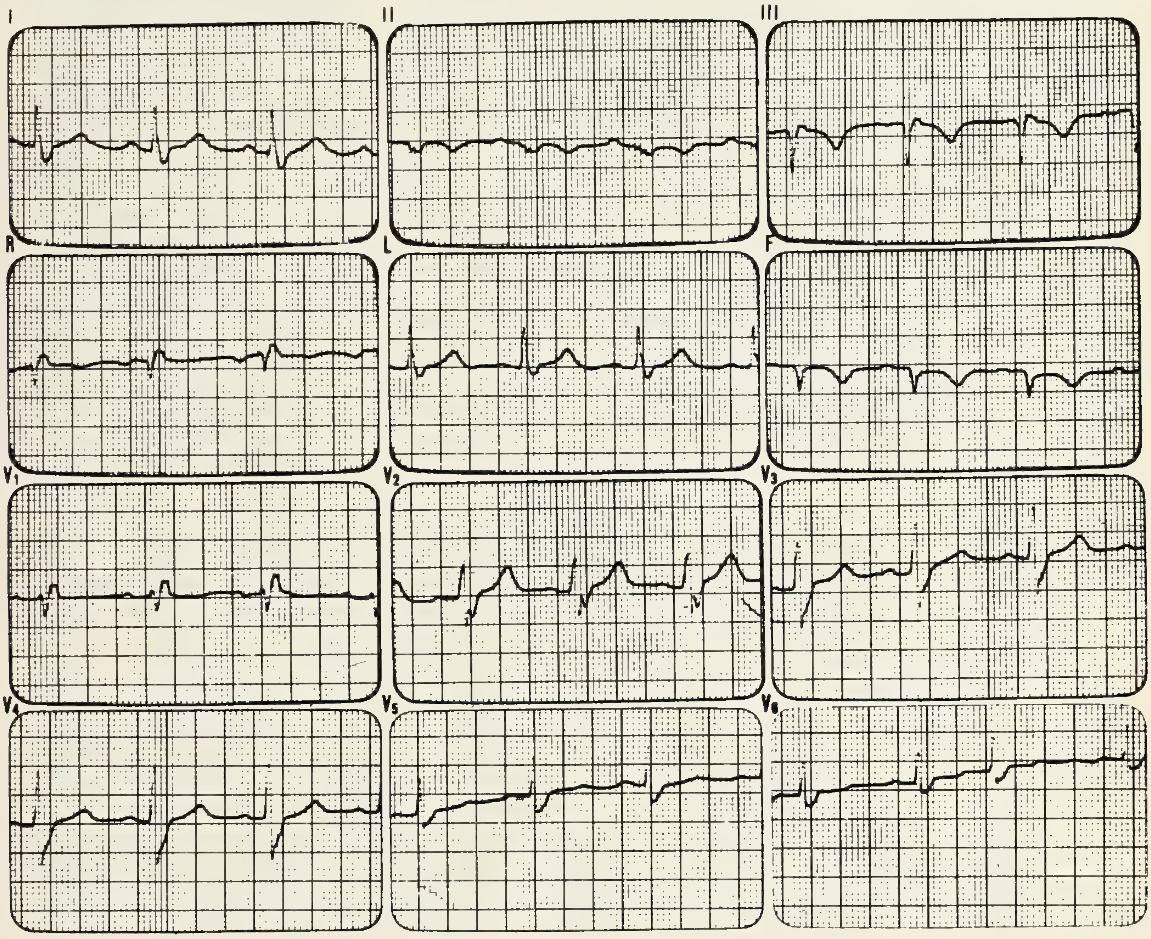
Figure 4 presents a normal ECG. Pertinent measurements and diagnosis have been transcribed from the complete computer report (Figure 2) to the bottom of the mounted tracing.

Figure 5A presents an ECG with a diaphragmatic myocardial infarction, right bundle branch block, and left axis deviation. The correct computer diagnosis was made even though lead 2 and lead V6 were not measured. This demonstrates the advantage of a computer diagnostic criteria which can scrutinize redundant signal information provided in the 12-lead ECG. The full computer report is shown. (Figure 5B)

(Figure 6A presents an ECG with anterior myocardial infarction of undetermined age and sinus tachycardia. The full computer report is shown. (Figure 6B)

Accuracy of Computer Diagnosis

In a recent Hartford Hospital study 400 ECGs were read both by computer and by two physicians independently.[5] The two physicians then, in consultation, reviewed their original reading and the computer reports to arrive at a "standard" interpretation. Most ECGs contain from one to six diagnostic statements. If all computer diagnoses agreed with the standard diagnoses, final complete agree-



HARTFORD HOSPITAL
DEPARTMENT OF MEDICINE EKG SCREENING PROJECT

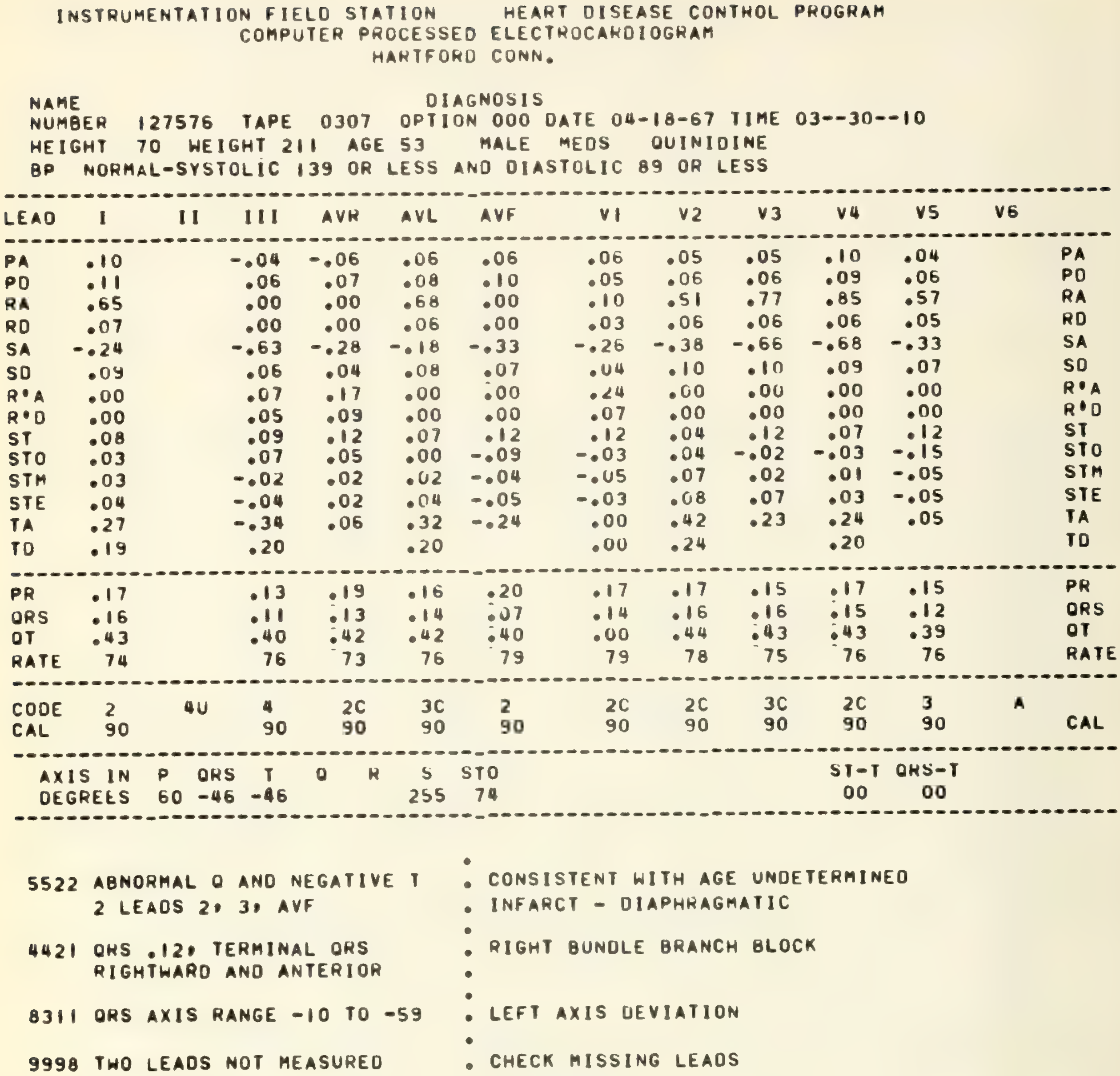
NAME 7576	AGE 53	LOCATION	HOSPITAL NUMBER	DATE 4-18-67
PR .17	QRS .16	QT .43	RATE & RHYTHM 74	MEAN QRS AXIS -46°

DESCRIPTION

```
Consistent with age undetermined infarct - diaphragmatic
Right bundle branch block
Left axis deviation
```

FIGURE 5A

Abnormal ECG showing diaphragmatic (inferior) myocardial infarction. Abbreviated computer interpretation is shown.



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      INSTRUMENTATION FIELD STATION     HEART DISEASE CONTROL PROGRAM
                      COMPUTER PROCESSED ELECTROCARDIOGRAM
                               HARTFORD CONN.

   NAME                                 DIAGNOSIS
   NUMBER  127576  TAPE  0307  OPTION 000 DATE 04-18-67 TIME 03--30--10
   HEIGHT  70  WEIGHT 211  AGE 53    MALE  MEDS   QUINIDINE
   BP  NORMAL-SYSTOLIC 139 OR LESS AND DIASTOLIC 89 OR LESS
---------------------------------------------------------------------------
LEAD   I      II    III    AVR    AVL    AVF      V1    V2    V3    V4    V5    V6
---------------------------------------------------------------------------
PA    .10          -.04   -.06    .06    .06     .06   .05   .05   .10   .04        PA
PD    .11           .06    .07    .08    .10     .05   .06   .06   .09   .06        PD
RA    .65           .00    .00    .68    .00     .10   .51   .77   .85   .57        RA
RD    .07           .00    .00    .06    .00     .03   .06   .06   .06   .05        RD
SA   -.24          -.63   -.28   -.18   -.33    -.26  -.38  -.66  -.68  -.33        SA
SD    .09           .06    .04    .08    .07     .04   .10   .10   .09   .07        SD
R'A   .00           .07    .17    .00    .00     .24   .00   .00   .00   .00        R'A
R'D   .00           .05    .09    .00    .00     .07   .00   .00   .00   .00        R'D
ST    .08           .09    .12    .07    .12     .12   .04   .12   .07   .12        ST
STO   .03           .07    .05    .00   -.09    -.03   .04  -.02  -.03  -.15        STO
STM   .03          -.02    .02    .02   -.04    -.05   .07   .02   .01  -.05        STM
STE   .04          -.04    .02    .04   -.05    -.03   .08   .07   .03  -.05        STE
TA    .27          -.34    .06    .32   -.24     .00   .42   .23   .24   .05        TA
TD    .19           .20           .20            .00   .24         .20              TD
---------------------------------------------------------------------------
PR    .17           .13    .19    .16    .20     .17   .17   .15   .17   .15        PR
QRS   .16           .11    .13    .14    .07     .14   .16   .16   .15   .12        QRS
QT    .43           .40    .42    .42    .40     .00   .44   .43   .43   .39        QT
RATE   74            76     73     76     79      79    78    75    76    76        RATE
---------------------------------------------------------------------------
CODE   2      4U     4     2C     3C      2      2C    2C    3C    2C    3     A
CAL   90             90     90     90     90      90    90    90    90    90        CAL
---------------------------------------------------------------------------
  AXIS IN   P  QRS   T    Q    R    S   STO                     ST-T  QRS-T
  DEGREES  60  -46  -46             255  74                      00    00
---------------------------------------------------------------------------

 5522 ABNORMAL Q AND NEGATIVE T   . CONSISTENT WITH AGE UNDETERMINED
      2 LEADS 2, 3, AVF           . INFARCT - DIAPHRAGMATIC
                                  .
 4421 QRS .12, TERMINAL QRS       . RIGHT BUNDLE BRANCH BLOCK
      RIGHTWARD AND ANTERIOR      .
                                  .
 8311 QRS AXIS RANGE -10 TO -59   . LEFT AXIS DEVIATION
                                  .
 9998 TWO LEADS NOT MEASURED      . CHECK MISSING LEADS
```

FIGURE 5B

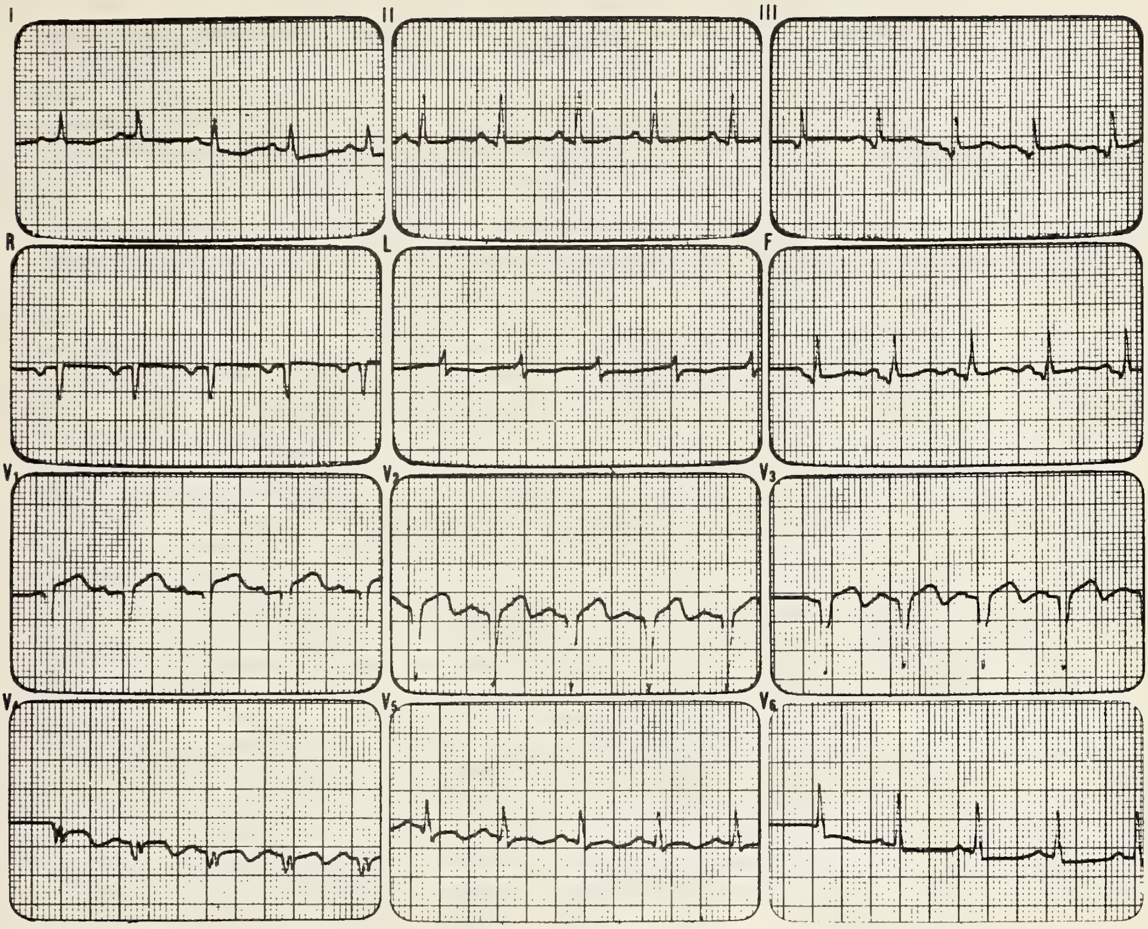
Full computer report of tracing shown in Figure 5A.

ment was noted. This occurred in 71% of tracings. Reports with minor disagreements which did not alter the overall sense of the report were noted in 14% of tracings. Thus in total, 85% of the reports were acceptable. In the tracings studied there were 611 "standard" diagnostic statements. Eighty-seven per cent (533/611) were correctly identified by computer.

"Major" ECG diagnoses were defined as ischemia, infarction, hypertrophy, conduction defects or marked ST segment deviation. In the study group of tracings there were 194 standard "major" diagnostic statements. The computer agreed with 91% of these diagnoses (177/194).

Limitations of Present Computer ECG Reports

Computer diagnostic sensitivity is achieved at the expense of some over-reading. This loss in specificity is due to the present adjustment of criteria so that even minor aberrations in the ECG waveforms are identified and labeled by the computer. In the Hartford Hospital study all abnormal ECGs were classified as abnormal by the computer. Not a single abnormal tracing was falsely labeled normal. On the other hand the computer falsely classified as abnormal 18.6% (21/113) of normal tracings. This indicates that the hospital physician must review all machine reports prior to clinical use. Be-



HARTFORD HOSPITAL
DEPARTMENT OF MEDICINE EKG SCREENING PROJECT

NAME 7582	AGE 63	LOCATION	HOSPITAL NUMBER	DATE 4-18-67

PR .11	QRS .10	QT .00	RATE & RHYTHM 111	MEAN QRS AXIS 41°

DESCRIPTION	Tachycardia Exclude ventricular PC Consistent with age undetermined infarct - anterior

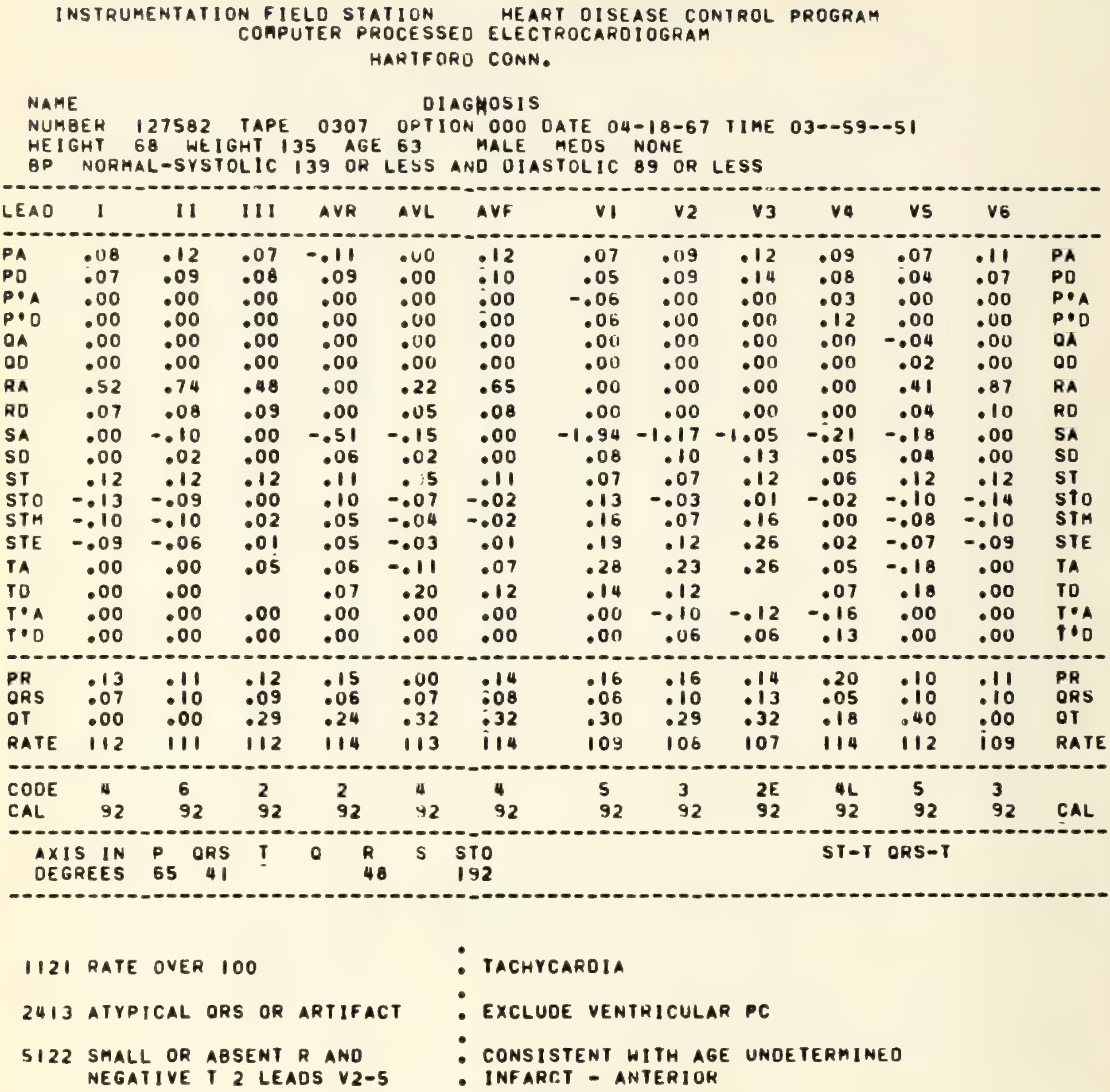
FIGURE 6A
Abnormal ECG showinf anterior myocardial infarction. Abbreviated computer interpretation is shown.

cause of the accuracy of ECGs reported as normal by computer, they may be subjected to very rapid physician review.

Serial tracing comparison and the precise differentiation of arrhythmias must presently be performed by physician readers. It is hoped that further computer programming will one day provide machine assistance in these important areas. Machine reports can provide objective measurements and interpretations of each tracing in a series which are considered to be useful to the physician who must presently make the comparisons.

Cost of Present System

Precise cost estimates are difficult because the system is in a developmental stage. Computer processing time has been provided by the Medical Systems Development Laboratory of the United States Public Health Service to aid the development of hospital and community use of computer ECG reports. Comparable computer hardware is being developed and should cost between $125,000-150,000. Rental of a comparable computer system might be obtained for $3,000-4,000 per month. Telephone transmission of electrocardiograms (Hartford—Washington) costs



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    INSTRUMENTATION FIELD STATION     HEART DISEASE CONTROL PROGRAM
                   COMPUTER PROCESSED ELECTROCARDIOGRAM
                              HARTFORD CONN.

  NAME                                 DIAGNOSIS
  NUMBER  127582  TAPE  0307  OPTION 000 DATE 04-18-67 TIME 03--59--51
  HEIGHT  68  WEIGHT 135  AGE 63    MALE  MEDS  NONE
  BP  NORMAL-SYSTOLIC 139 OR LESS AND DIASTOLIC 89 OR LESS
-----------------------------------------------------------------------------
LEAD    I     II    III    AVR    AVL    AVF      V1    V2    V3    V4    V5    V6
-----------------------------------------------------------------------------
PA     .08   .12   .07   -.11    .00    .12      .07   .09   .12   .09   .07   .11   PA
PD     .07   .09   .08    .09    .00    .10      .05   .09   .14   .08   .04   .07   PD
P'A    .00   .00   .00    .00    .00    .00    -.06   .00   .00   .03   .00   .00   P'A
P'D    .00   .00   .00    .00    .00    .00      .06   .00   .00   .12   .00   .00   P'D
QA     .00   .00   .00    .00    .00    .00      .00   .00   .00   .00  -.04   .00   QA
QD     .00   .00   .00    .00    .00    .00      .00   .00   .00   .00   .02   .00   QD
RA     .52   .74   .48    .00    .22    .65      .00   .00   .00   .00   .41   .87   RA
RD     .07   .08   .09    .00    .05    .08      .00   .00   .00   .00   .04   .10   RD
SA     .00  -.10   .00   -.51   -.15    .00   -1.94 -1.17 -1.05  -.21  -.18   .00   SA
SD     .00   .02   .00    .06    .02    .00      .08   .10   .13   .05   .04   .00   SD
ST     .12   .12   .12    .11    .05    .11      .07   .07   .12   .06   .12   .12   ST
STO   -.13  -.09   .00    .10   -.07   -.02      .13  -.03   .01  -.02  -.10  -.14   STO
STM   -.10  -.10   .02    .05   -.04   -.02      .16   .07   .16   .00  -.08  -.10   STM
STE   -.09  -.06   .01    .05   -.03    .01      .19   .12   .26   .02  -.07  -.09   STE
TA     .00   .00   .05    .06   -.11    .07      .28   .23   .26   .05  -.18   .00   TA
TD     .00   .00          .07    .20    .12      .14   .12         .07   .18   .00   TD
T'A    .00   .00   .00    .00    .00    .00      .00  -.10  -.12  -.16   .00   .00   T'A
T'D    .00   .00   .00    .00    .00    .00      .00   .06   .06   .13   .00   .00   T'D
-----------------------------------------------------------------------------
PR     .13   .11   .12    .15    .00    .14      .16   .16   .14   .20   .10   .11   PR
QRS    .07   .10   .09    .06    .07    .08      .06   .10   .13   .05   .10   .10   QRS
QT     .00   .00   .29    .24    .32    .32      .30   .29   .32   .18   .40   .00   QT
RATE   112   111   112    114    113    114      109   106   107   114   112   109   RATE
-----------------------------------------------------------------------------
CODE    4     6     2      2      4      4        5     3     2E    4L    5     3
CAL     92    92    92     92     92     92       92    92    92    92    92    92   CAL
-----------------------------------------------------------------------------
  AXIS IN   P  QRS   T    Q    R    S   STO                   ST-T QRS-T
  DEGREES  65   41             48       192
-----------------------------------------------------------------------------


  1121 RATE OVER 100                 .
                                     . TACHYCARDIA
                                     .
  2413 ATYPICAL QRS OR ARTIFACT      . EXCLUDE VENTRICULAR PC
                                     .
  5122 SMALL OR ABSENT R AND         . CONSISTENT WITH AGE UNDETERMINED
       NEGATIVE T 2 LEADS V2-5       . INFARCT - ANTERIOR
```

FIGURE 6B

Full computer report of tracing shown in Figure 6A.

$1.25/ECG and teletyping of reports (Washington to Hartford) costs $.80-1.60 per ECG report depending on the length of the report. Rented (private) phone and teletyping lines are far more practical when more than 500 ECGs per month are to be transmitted. Cost of rental of phone transmitters and receivers is nominal (See Table I). Magnetic tape ECG data acquisition carts at $6,400 each represent a large initial capital outlay. Considering a volume of about 3500 ECGs/cart/year for an estimated five years, this item can be said to add a $.37 cost per ECG.

Equipment maintenance costs must be figured in as well. ECG technician salaries and physician reader salaries will remain similar to previous costs for these services prior to use of the automated system. However, physicians should accomplish a greater volume of work per unit of time.

Comment

The Hartford Hospital project represents the first routine use by a community hospital of telephone transmission of ECGs for remote computer analysis. Local telephone transmission of ECGs for computer analysis is feasible and has been previously reported.[6] The present report deals with routine telephone transmission of ECGs over a distance of 340 miles.

Current project work in the Hartford Hospital Emergency Room has demonstrated for the first time that immediate "on-line" computer processing and teletype reporting of ECG diagnosis is feasible.

Other investigators have explored computer analysis of ECGs. A system has been developed employing telephone transmission of ECGs from Massachusetts Memorial Hospital to a computer center at Massachusetts Institute of Technology.[7,8,9] A General Electric 225 digital computer is employed. A single ECG lead (Frank system lead X) is transmitted and analyzed. A multiple adaptive "matched filter" technique is employed in the ECG pattern recognition program. The final report teletyped to the hospital inclules a statement of rhythm, wave measurements, QRS pattern classification, and final ECG diagnosis. In addition they have been working with computer diagnosis of simultaneously recorded X, Y, Z corrected orthogonal Frank leads.

At the Washington, D.C. Veterans Administration Hospital, Pipberger of Georgetown University Department of Medicine, has developed a functioning digital computer program for routine ECG analysis of X, Y, Z corrected orthogonal Frank leads.[10,11] The system has employed off-line computation by an IBM 7094 computer. At the Mayo Clinic 12-lead Scalar ECGs and modified Frank lead ECGs are currently recorded for automated processing. An on-site IBM computer analyzes only the modified Frank leads to print a diagnosis. A number of other investigators have been contributing to progress in this rapidly expanding field.

The Medical Systems Development Laboratory ECG analysis program provides accurate measurement and diagnostic interpretation.[12] The program analyzes traditional 12-lead ECGs and diagnostic terminology is familiar to most physicians. These factors make the program very suitable for use by a community hospital.

Acknowledgment

The authors acknowledge the technical assistance of Mrs. Sheila I. Brown in the conduct of the project and in preparation of this manuscript.

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TABLE I

EQUIPMENT UTILIZED IN AUTOMATED ELECTROCARDIOGRAPHY PROJECT

At Hartford, Connecticut

1. ECG data acquisition carts: "Dat-EK" carts built by Computer Instruments Corporation, Hempstead, L.I., New York. (Approx. cost $6,400 each)
2. Data-phone transmitter: Bell Telephone Model X603A built by Western Electric. (Rental $25 per month)
3. Phone communication: Rented private line.
4. Teletype machine: Model 33KSR built by Teletype Corporation. (Rental $45 per month)

At Washington, D.C., Medical Systems Development Laboratory, Heart Disease Control Program

1. Data-phone receiver: Bell Telephone Model X603B built by Western Electric. (Rental $25 per month)
2. Cardiac data input console: With input tape decks, krohnhite filters, oscillographic monitoring, and 2 channel analogue to digital computer designed and built by Medical Systems Development Laboratory and Airborne Instruments Laboratories, Long Island, New York. Specifications for a suitable 8 channel input console system (DEC Corporation, Maynard, Massachusetts) can be obtained from the Medical Systems Development Laboratory, Washington, D.C.
3. Computer: Control Data Corporation 160-A digital computer with additional memory totaling 16K. The ECG program was originally written in machine language and contains some 12,000 instructions. The program is currently in OSAS format.

4. CDC paper tape reader and punch.
5. CDC 165 plotter used for digital-to-analogue conversion for program validation.
6. CDC 166 high speed line printer.
7. Four CDC 163 magnetic tape drives used to store diagnostic programs for the computer and format the computer results.
8. Teletype machine: Model 35ASR.

KNOWLEDGE AND IGNORANCE, PRIDE AND POWER

Absolute knowledge could, therefore, leave nothing outside itself; and only on condition of knowing everything could man be granted its attainment. Man behaves as if he were destined to reach this absolute knowledge; and the incessant *why* which he puts to nature proves it. Indeed, this hope, constantly disappointed, constantly reborn, sustains and always will sustain successive generations in passionate search for truth.

Our feelings lead us at first to believe that absolute truth must lie within our realm; but study takes from us, little by little, these chimerical conceits. Science has just the privilege of teaching us what we do not know, by replacing feeling with reason and experience and clearly showing us the present boundaries of our knowledge. But by a marvellous compensation, science, in humbling our pride, proportionately increases our power. Men of science who carry experimental analysis to the point of relatively determining a phenomenon doubtless see clearly their own ignorance of the phenomenon in its primary cause; but they have become its master; the instrument at work is unknown, but they can use it. This is true of all experimental sciences in which we can reach only relative or partial truths and know phenomena only in their necessary conditions. But this knowledge is enough to broaden our power over nature. Though we do not know the essence of phenomena, we can produce or prevent their appearance, because we can regulate their physico-chemico conditions. We do not know the essence of fire, of electricity, of light, and still we regulate their phenomena to our own advantage. We know absolutely nothing of the essence even of life; but we shall nevertheless regulate vital phenomena as soon as we know enough of their necessary conditions. Only in living bodies these conditions are much more complex and more difficult to grasp than in inorganic bodies; that is the whole difference.—CLAUDE BERNARD, M.D. *An Introduction to the Study of Experimental Medicine.* New York, The Macmillan Company, 1927, p. 82.

The Clinical Value Of The Esophageal Acid Perfusion Test In Patients With Chest Pain*

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Introduction

The two most common disorders causing retrosternal and precordial pain are esophagitis and coronary artery disease. At times, the differential diagnosis of these entities remain an enigma. Recent advances in esophageal and cardiac diagnostic aids have helped to solve some of these difficult diagnostic problems. In 1958, Bernstein introduced the acid perfusion test (APT) which consisted of a constant perfusion of 0.1 N HC1 into the distal esophagus.[1] A correlation of the test in patients with symptoms of chronic esophagitis was excellent, but unfortunately, this simple procedure has not gained wide use.

The present paper describes our recent experience with this test as a diagnostic aid; simultaneous recording of pH values during the acid perfusion and while neutralization was performed with antacid; and correlation with patients whose cardiac status warranted a selective coronary artery angiogram (SCA).

Methods

Four asymptomatic subjects and 16 symptomatic patients had the following studies performed as inpatients or out-patients at the Norwalk Hospital. 1) An electrocardiogram; 2) routine upper gastrointestinal radiographic barium study which included fluoroscopic evaluation of the cardio-esophageal junction; and 3) an acid perfusion test (APT) as described by Bernstein.[1] First saline, then 0.1 N HC1, then again saline was dripped through polyethelene tubing which was positioned in the esophagus at 33-35 centimeters from the lips. Solutions were administered from intravenous bottles at a rate of 100-120 drops per minute for 15-30 minutes. The criteria for a positive pain response were as described by Bernstein.[1] Patients were unaware of which bottle was being administered. When pain was elicited, the final solution used was 30-60 ml. of an aluminum hydroxide-magnesium trisilicate antacid (GELUSIL). The test was modified by attaching a glass electrode to the polythelene tubing. A reference electrode was held by the patient and recordings of pH made by a Beckman Zeromatic meter. pH recordings were made while the subjects were at rest, after bending over, during forced expiration against a closed epiglottis, and during all perfusions.

Three patients, Nos. 12, 13 and 14 had selective coronary arteriography (SCA)[2] and one patient esophagoscopy with a Lopresti flexible esophagascope. The low incidence of endoscopy was due to the high index of negative esophagrams and positive electrocardiograms.

Results

The results on each patient are recorded in Table I. The correlation of symptoms and clinical diagnosis with positive acid perfusion tests and positive myocardial disease tests (ECG or SCA) are recorded in Table II.

All 4 control subjects had no pain elicited during acid perfusion. Of the 16 symptomatic patients, 5 had significant pain with acid perfusion that relented with saline and was relieved by antacid perfusion.

All of the patients with positive acid perfusion tests had hiatus hernias on radiographic study. Four had so-called "heart-burn" (defined as a precordial burning sensation), as their presenting symptom and one a dull precordial pain which presented as a diagnostic problem.

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* *This work was supported in part by a grant from the Warner-Chilcott Laboratories through the cooperation of Mr. Tom Bastyr and the United States Public Health Service Grant No. 0700-9A-67 from the Cancer Control Branch of the Division of Chronic Diseases.*

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Two patients had acid reflux as measured by the esophageal glass electrode. One had a hiatel hernia with heartburn and a positive APT (Case 18) and the other hiatal hernia with heartburn but a negative APT (Case 7). Of the other three patients with hiatus hernias and negative perfusion tests, two had xiphoid pain (Cases 5 and 8) and one (Case 13) precordial pain which was established as due to diffuse coronary disease by SCA.

Four patients had confirmatory evidence of active myocardial disease (Cases 11, 12, 13 and 15), two by SCA and two by electrocardiogram. Two had presented with dysphagia and two with precordial pain. All had negative perfusion tests, although one had a hiatus hernia.

Case No. 6 had presented with dysphagia and a negative APT but a positive esophageal biopsy for carcinoma although the x-ray diagnosis was equivocal.

Of the three cases that had selective coronary angiography, all three had negative perfusion tests, two had coronary artery disease (Cases 12 and 13).

Case No. 13 illustrated a typical diagnostic problem. The patient presented with vague persistent recurrent nocturnal precordial pain, a normal ECG and a hiatus hernia on radiographic study. The evidence of no reflux by pH measurement, a negative APT and a positive SCA established the diagnosis as pain due to coronary artery disease.

Table I

Patient	Sex	Age	C.C.	X-Ray	Fall in pH After Straining	Symptoms With HCl	APT Result	Positive ECG or SCA
1	M	26	Asympt.	Neg.	None	None	Neg.	——
2	M	27	Asympt.	Neg.	None	None	Neg.	——
3	M	27	Asympt.	Neg.	None	None	Neg.	——
4	F	25	Asympt.	Neg.	None	None	Neg.	——
5	M	63	Epig. Pain	Hiatus Hernia	None	None	Neg.	——
6	M	73	Dysphagia	Narrow Lower Esoph.	None	None	Neg.	——
7	M	49	Epig. Pain, Heartburn	Hiatus Hernia Esoph. Ring Duod. Ulcer	Yes	None	Neg.	——
8	F	58	Epig. Pain	Small Hiatus Hernia	None	None	Neg.	——
9	F	52	Heartburn	Neg.	None	None	Neg.	——
10	M	75	Substernal Pain	Curled Esoph	None	None	Neg.	——
11	M	65	Substernal Burning Pain	Neg.	——	None	Neg.	——
12	M	44	Dysphagia	Neg.	None	None	Neg.	SCA—Mild Coronary Artery Disease
13	F	64	Precordial Pain	Small Hiatus Hernia	None	None	Neg.	SCA-Severe Coronary Artery Disease
14	F	50	Precordial Pain	Small Divert. 2nd Duod.	None	None	Neg.	SCA—Neg.
15	F	61	Dysphagia Anxiety	Neg.	None	None	Neg.	EKG—Myocardial Infarction
16	M	44	Heartburn	Hiatus Hernia	None	Heartburn	Pos.	——
17	M	47	Substernal Pain	Small Hiatus Hernia	None	Substernal Pain	Pos.	——
18	M	46	Heartburn	Small Hiatus Hernia	Yes	Heartburn Epig. Pain	Pos.	——
19	F	55	Heartburn	Esoph. Ring Hiatus Hernia	None	Heartburn	Pos.	——
20	F	69	Substernal Pain, Heart burn	Small Hiatus Hernia	None	Substernal Pain, Heartburn	Pos.	ECG = Old Myocardial Infarction

Discussion

The present study demonstrates the value of the acid perfusion test in refining the diagnosis of retrosternal or precordial pain. All patients in this study that had a positive test had radiographic evidence of hiatal hernia. Several patients with hiatus hernia had negative tests. The presence of a positive APT usually indicates esophagitis. This correlation was documented in the original work of Bernstein[1] and confirmed by several other authors[3,4]. Although hydrochloric acid induces pain, the positive acid perfusion test does not always indicate that the esophagitis is due to acid reflux from the stomach, for alkaline reflux may also give the same symptoms. A symptom produced by artificial hydrochloric acid perfusion merely indicates a susceptible or diseased mucosa. However, in most cases, the symptom of heartburn is due to acid reflux. This type of reflux has been clearly demonstrated in patients with hiatus hernia[4,5] and during prolonged intubation[6], but it is not associated with any clear esophageal motility disturbance[6]. Although the APT was positive in these patients, we were only able to demonstrate acid reflux on pH determination in one of the patients. Both Tuttle and colleagues[3,5], and Weber and Gregg[4] were able to demonstrate reflux with ease in their patients with hiatus hernia and positive perfusion tests. We are unable to explain why our recordings did not demonstrate reflux in a high percentage of the cases. Although esophagitis is associated with reflux, reflux alone does not always mean esophagitis is present. An example of this was Case No. 7.

Coronary artery disease may present with symptoms indistinguishable from esophagitis. Of particular help in accurately defining the disease process at fault is the combination of the acid perfusion test with selective coronary angiography. The following cases demonstrate the clinical value of these tests. Case 13, who had precordial pain, a negative APT, had severe coronary artery disease on SCA. In cases No. 12 and 14, both the APT and SCA were negative. The fear of coronary artery disease was relieved and unnecessary treatment for esophagitis avoided. Case No. 11 had a negative APT but ischemic heart disease on electrocardiogram which obviated the need for angiography.

The acid perfusion test in the evaluation of retrosternal and precordial pain is a valuable addition to the diagnostic armamentorium. In conjunction with electrocardiographic studies and in selective cases, esophagoscopy and selective coronary angiography most problems in the differential diagnosis of chest pain can be resolved easily.

TABLE II

RESULTS IN ACID PERFUSION TESTS AND CLINICAL CORRELATION IN 20 SUBJECTS

	#	*Pos. APT**	*Neg. APT*	*Pos. MD***
Asymptomatic Controls	4	0	4	0
Symptomatic Patients	16	5	11	4
Hiat. Hernia	9	5	4	1
pH Reflux	2	1	1	0
CA-Dysphagia	1	0	1	0
Epigastric Pain	2	0	2	0
"Heartburn"	6	4	2	0
Dysphagia	2	0	2	2
Precordial Pain	5	2	4	2
pH Reflux	2	1	1	0

*APT = Acid Perfusion Test (See Methods)
**MD = Active Myocardial Disease

Summary

Four normal subjects and 16 patients were studied with the acid perfusion test to differentiate the cause of retrosternal or precordial pain. Five patients had a positive test and evidence of haitus hernia. Their symptoms correlated well with the diagnosis of esophagitis. In problem cases, the use of electrocardiographic studies and selective coronary angiography demonstrated the etiology of the pain when the acid perfusion tests were negative. It is felt that the simple HCl perfusion test is a helpful diagnostic aid in the differential diagnosis of chest pain.

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Organization Of A Four-bed Coronary Care Unit At The Hospital Of St. Raphael

A Teaching Community Hospital of New Haven

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Coronary artery disease is a leading cause of death in the United States, claiming 1,500 persons daily.[1] Death frequently results from (1) Myocardial failure, gradual deterioration and expected death from shock, heart failure, and terminal arrhythmias, or (2) serious arrhythmias and sudden, unexpected death. To minimize the danger of sudden death, intensive care units have been developed for close supervision and intensive nursing care of patients with myocardial infarction.

Danger of sudden death is particularly high at the moment of myocardial infarction and immediately thereafter. One out of five patients may not reach the hospital alive as shown in the Framingham study.[2] Danger of sudden death is ever present even in the hospital. In our cooperative study[3] of the death rate of 795 patients after myocardial infarction, 9.6% died during the first four days. In days 5 to 7, an additional 3.6% died. Of every 100 patients with acute myocardial infarction admitted to the hospital, 12 could be expected to die in the first week in the hospital while 30 would be expected to be dead at the end of one year. The Coronary Care Unit is directed toward the salvage of these deaths in the first week of hospitalization.

The Hospital of St. Raphael is a teaching community hospital with 462 adult beds, of which 124 are medical. The purpose of the Coronary Care Unit was to monitor, study, and give the best possible care to the patient with acute myocardial infarction, under supervision of highly trained and specialized nurses. Immediate treatment was directed to prevent the progression of initially harmless arrhythmias to fatal arrhythmias. The purpose of this paper is to report the first two years experience in this Unit.

Personnel Of Unit

The Coronary Care Unit is under the direction of one physician. Policy is determined in cooperation with the administrator of the hospital, the director of medicine, the supervisor of nurses, and the head nurse of the Unit. The Director visits the Unit at least once daily and is responsible for the continued education of the nursing and resident staff in the Unit. His decision is final in matters of admission and discharge.

Prior to the opening of the Coronary Care Unit nurses were intensively trained in all phases of myocardial infarction, in recognizing and interpreting arrhythmias (on the monitor and the electrocardiogram), in the use of cardiac drugs, and they received theoretical and practical instructions in resuscitation and defibrillation. One or two nurses are in constant attendance in the Unit. One of several second-year residents trained in handling cardiac emergencies in myocardial infarction is assigned as a research assistant to the Unit and is in immediate charge of all emergencies. Until his arrival, however, the nurses are instructed to defibrillate the unconscious patient and, in cases of cardiac arrest, to start cardiac massage and artificial respiration. Since the opening of the Unit all of the specially prepared nurses have successfully assisted at cardiac emergencies. One example of such an emergency successfully treated by the head nurses of the Unit is shown in Figure 1.

Since the time the Unit opened there were three resignations. These were due to marriage. Two nurses married two residents assigned to the Unit.

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This study was supported by Grant HE-06672 from the National Heart Institute

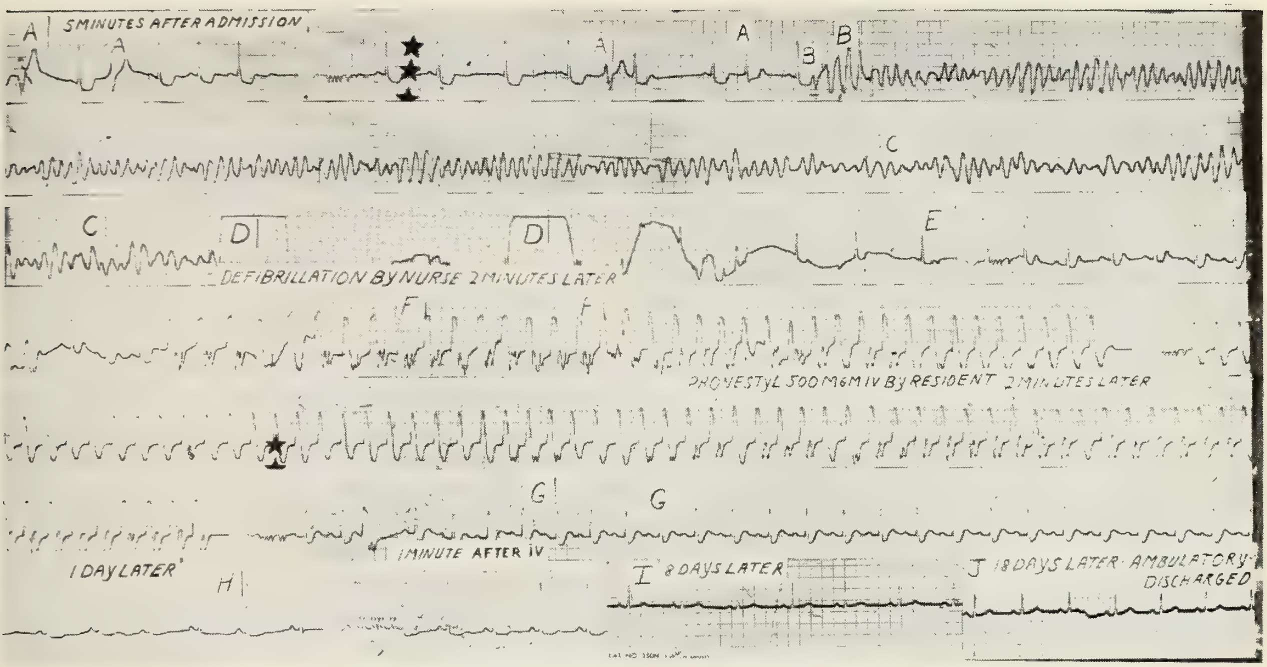
A 5 MINUTES AFTER ADMISSION
A
A
A
A
B
B
C
C
D
D
DEFIBRILLATION BY NURSE 2 MINUTES LATER
E
F
F
PRONESTYL 500 MGM IV BY RESIDENT 2 MINUTES LATER
G
G
1 MINUTE AFTER IV
1 DAY LATER
H
I 8 DAYS LATER
J 18 DAYS LATER · AMBULATORY · DISCHARGED

FIGURE I (Continuous Monitor Strip)

5 Minutes After Admission To Coronary Care Unit.

A. Dangerous Premature Beats (Multifocal, Numerous, Close To T Waves) As Shown On Memory Loop Strip.
B. Premature Ventricular Beat Close To Vulnerable Period Of T Wave Starts Run Of Ventricular Tachycardia. High Rate Alarm Alerts Nurse.
C. Ventricular Fibrillation With Cardiac Arrest.
D. Defibrillation By Nurse With 400 Watt/Sec. D. C. Current.
E. Sinus Rhythm After Defibrillation. Patient Is Conscious.
F. Ventricular Tachycardia, Broken With 500 mg. Pronestyl I.V. Slowly By Resident.
G. Sinus Rhythm With Bundle Branch Block After Pronestyl Treatment.
H. Sinus Rhythm Without Bundle Branch Block One Day Later.
I. Sinus Rhythm 8 Days Later. Patient Is Doing Well, Sitting Up.
J. Sinus Rhythm 18 Days Later. Patient Is Ambulatory And Discharged.

(Proving the value of the Unit in at least one matter of heart.) Loss of nursing personnel must be anticipated. To assure continued proper function of a Unit from loss of nursing personnel, courses of instruction must be repeated at least every six months for new nurses. Thirteen of such four weeks courses are given at present throughout the year at the Hospital of St. Raphael available to nurses from anywhere in the U.S.A. under a U.S. Public Health Service contract.

Private patients are under the care of their own physicians whose orders are carried out. Such patients are seen by the Director only at the request of the private physician. Ward patients are under the care of the resident, supervised by the attending physician on service and the Director of the Coronary Care Unit. Medical residents are required to remain in the Unit or in its vicinity, sleep in the Unit, and always carry a special electronic page. A resuscitation team consists of another second-year resident, an inhalation therapist, and a nurse's supervisor. They are instructed never to leave the hospital section in which the Coronary Care Unit is located unless they transfer their electronic page to another responsible person. In case of cardiac arrest, the nurse in the Coronary Care Unit activates this page by pressing an alarm button. Similar teams with special electronic pages are assigned to other sections of St. Raphael's Hospital for cardiac emergencies outside the Coronary Care Unit. If this electronic page fails (the nurse who initiates the alarm does not hear the buzzing on her own page), the hospital telephone operator is alerted to announce the location of the emergency over the loudspeaker.

Admission Policy To The Coronary Care Unit

Patients are admitted directly to the Coronary Care Unit. The private physician calls the nurse in charge of the Unit, rather than notifying the Admitting Office, to avoid delay. Any patient, private or ward, suspected of having a myocardial infarction is admitted to the Unit if space is available. Patients may be admitted by ambulance directly to the Unit, or through the Emergency Room or from any part of the hospital. Patients stay in the Unit at least 96 hours unless myocardial infarction is disproved. Routine transfers are between 9 a.m. and 7 p.m. Patients are prepared for transfer by assuring them that their condition has improved to such an extent that further close supervision is unnecessary. If a patient develops a life-threatening arrhythmia requiring defibrillation, resuscitation, or intensive drug treatment, he is kept at least four more days after the complication since arrhythmias tend to recur and may be fatal.

A special nursing unit with 16 additional beds is adjacent to the Coronary Care Unit, reserved for patients with myocardial infarction for whom there was no room in the Unit or who were transferred from the Unit after a minimum stay of four days. The usual hospital stay of patients who have acute myocardial infarctions averages 3 weeks of which 4 days are spent in the Coronary Care Unit and 17 days in the adjacent special nursing division.

The Unit And Equipment

Patients are separated from each other by fairly soundproof walls, built mostly of glass, so designed that the patient's view of the adjoining room is blocked but the nurse can observe all patients at all times. Each of the four rooms in the Unit is fully equipped with a noiseless monitor, oxygen outlets, wall suction, bedside commode, calendar with large letters and figures, a stop clock, an electrically controlled bed with a cardiac board and infusion pole, wall sphygmomanometer and stethoscope, and the previously mentioned two alarm systems.* Electrical outlets are wired for the usual power source and auxiliary emergency supply. Each room contains an individual thermostat and air conditioning. Within the Unit is a defibrillator, cardioverter, automatic tourniquet machine, intermittent positive pressure machine, a battery-powered pacemaker with sterile intracardiac electrodes and disposable sets for central venous pressure. The supplies and machines are checked regularly.

Utilization

In two years 596 patients were admitted to the Unit with suspected acute myocardial infarction. Average stay in the Unit was four days. Average occupancy was 72% of capacity. All four beds were occupied a total of 257 days. On only 19 days in the entire two years was the Unit empty. The majority of these 19 days were during July and August when the incidence of myocardial infarction usually is low in the eastern part of the USA. (A good time to plan staff vacation!). In certain months, however, admission had to be refused for lack of space.

Treatment

Every private patient remains under the care of the private physician who visits and writes orders for his patient daily. He is promptly informed of any change in his patient's condition by the nurse in charge or the resident on duty. The resident, in turn, carries out the given orders after discussing the patient's condition with the private physician. In case of any emergency, however, the nurse and, if present, the resident will immediately institute life-saving techniques including defibrillation and cardiac massage until the patient's private physician arrives. The Director of the Unit also is available for consultations. Ward patients are treated by the resident of the Unit, supervised by the attending physician and, on request, in consultation with the Director of the Unit.

On arriving at the Unit, every patient is immediately attached to a monitor, an I.V. infusion is started with an Intracath to keep the vein open. On several occasions, life-threatening emergencies have occurred shortly after arrival and immediate monitoring allowed the detection of arrhythmias and life-saving treatment (Figure 1).

Various antiarrhythmic drugs, alone or in combination as indicated, are given promptly if any of the following major arrhythmias occur:

1. Atrial fibrillation or flutter
2. Atrial tachycardia, or more than 6 premature atrial contractions per minute
3. Nodal tachycardia or nodal rhythm
4. Ventricular tachycardia
5. Ventricular fibrillation or ventricular flutter
6. Idioventricular rhythm
7. After emergency cardioversion of any arrhythmia
8. Ventricular standstill
9. Premature ventricular beats, of more than 6 per minute, of multifocal origin, in coupled rhythm, or occurring on the downstroke of the T-wave
10. Marked sinus bradycardia

Patients admitted without arrhythmias or with premature beats less than six per minute who are not in shock, do not have intractable vomiting, and do not show AV or bundle branch block are treated according to a protocol of a cooperative study[4] of which the Coronary Care Unit of the Hospital of St. Raphael is a participant: If Pronestyl is given, the dose every 4 hours for 24 doses is 500 mg. if the patient weighs less than 180 pounds and 750 mg. if over 180 pounds. After the 24th dose the same amount is continued every 6 hours. If Quinidine is given, the initial dose is 0.4 gm., followed by 0.2 gm. every four hours if the body weight is 150 pounds or less; 0.2 gm. every 3 hours if the weight is 150 to 200 pounds and 0.2 gm. every 2 hours if the weight is 200 pounds or more. After the 5th dose everybody receives 0.2 gm. every 6 hours, but this amount is adjusted to maintain the Quinidine blood level between 4-8 mg/L., as determined daily. Quinidine is omitted if the BUN rises above 25 since the breakdown products are retained and interfere with the blood tests for Quinidine.

---

* The monitoring equipment, defibrillators and pacemakers are made by General Electric Co.; the paging system made by Motorola.

Patients with serious arrhythmias are treated aggressively with either intravenous Pronestyl, Lidocaine, cardiac glycosides, Dilantin or Isoproterenol depending on the type of arrhythmia. Quinidine is mostly used orally or intramuscularly, never intravenously as an injection, but is occasionally used in an infusion with constant monitoring of cardiac rhythm and blood pressure. In the presence of frequent premature ventricular contractions particularly if multifocal or close to the downstroke of the preceding T waves, or if there are short bursts of ventricular tachycardia, or persistent ventricular tachycardia, 50-75 mg. of the short-acting antiarrhythmic Lidocaine is injected intravenously as a bolus. The same dose is repeated in about 2-10 minutes if necessary. The dosage varies with the body weight. If the arrhythmias are suppressed with the direct injection of the drug 500 to 1,000 mg. of Lidocaine is used as a continuous microdrip in 475 or 450 cc 5% glucose in distilled water. This intravenous microdrip is used to prevent recurrence of arrhythmia rather than to suppress already existing arrhythmia. About 1-2 mg. per minute is administered. In desperate cases this dosage was increased for a short period up to 4 mg. per minute. The rate of drip is increased if extra beats recur and slowed down if they disappear. At the same time either Pronestyl or Quinidine is started orally, according to weight. In heart block, Lidocaine, Pronestyl, and Quinidine are best omitted. With the use of Lidocaine blurred vision, muscle contraction, inability to speak, nausea and vomiting and sensation disorder were seen in a few patients. Other reported side reactions such as euphoria, dysphagia, and dyspnea mentioned by Barnett[6] were not noticed. Even if Lidocaine fails, Procaine Amide (Pronesty®) was successful when 100 mg. was injected in the first minute (diluted in 5% Dextrose in water) followed by 50-100 mg. every minute until the arrhythmia is suppressed. The blood pressure and cardiac monitor are carefully watched for a drop in pressure, undue widening of the QRS complexes, or change in rhythm. If the blood pressure drops or is low at the beginning of the arrhythmia, Levofed 4 mg. in 500 cc. of 5% Dextrose in distilled water or 100 mg. of Metaraminol (Aramine) in 500 cc. of 5% Dextrose in distilled water is given. Raising the blood pressure alone may terminate supraventricular arrhythmias. Widening of the QRS complexes for more than 30 beats by more than 50% of their previous duration was considered an indication to terminate Pronestyl at least temporarily until the pressure was restored or the widening of the QRS complexes had subsided. At times a combination of these drugs is used. If response to one or a combination of these drugs is not prompt in a life-threatening arrhythmia (particularly if the patient shows signs of shock secondary to arrhythmia), electrical cardioversion with direct current is used either without anesthesia or preceded by intravenous Valium,® dependent on the urgency of the procedure and the condition of the patient.

If first or second degree heart block is present 0.8-1 mg. atropine is injected intravenously in the course of two minutes and it is repeated every 2-4 hours as needed. If it fails Isoproterenol 2 mg. in 500 cc. of 5% glucose in distilled water is used and an intravenous microdrip to increase the ventricular rate to 60-80 beats per minute. At times intravenous steroids were used, in addition. Transvenous pacemakers were not inserted for first or second degree block, but only for complete heart block, which did not readily respond to atropine or Isoproterenol.

Cardiogenic shock, manifested by low blood and pulse pressure, restlessness or impaired sensorium, pale cold moist skin, collapsed veins, oliguria, poor capillary filling, marked bradycardia or tachycardia, is treated immediately and vigorously as soon as recognized. Arrhythmias are treated as previsously described. When corrected, the shock may subside and the patient improves immediately, but only if the shock was produced by the arrhythmia. If the arrhythmias were produced by long-standing shock, their correction will not improve the patient's shock. Such arrhythmias are usually preterminal. All treatment is extremely discouraging and most patients will die despite all present day treatment.

Nevertheless, all patients with Cardiogenic Shock are treated vigorously. Patients previously not digitalized receive digitalis glycosides intravenously: Ouabain 0.5 mg. is given slowly in 3-5 minutes under close observation of the rhythm on the monitor. In old patients, only 0.25 mg. is given. Additional 0.125 mg. are given every hour for several doses until a maximum total of 1 mg. in 24 hours is injected or the therapeutic or toxic endpoint is reached. In posterior wall infarcts, more prone to heart block or in old patients, usually 0.75 mg. is the maximum dose, unless frank failure persists. Usually the patient is then simply maintained on Digoxin 0.25 mg. daily. If necessary, 0.5-0.75 mg. per os is given for one or two days. Old patients, or patients with a high BUN usually receive only 4-5 doses weekly to prevent digitalis excess. Other physicians in the Unit, however, use either intravenous Cedilanid or Digoxin initially. Ouabain is not used if the patient has received any other Digitalis preparation within the last two weeks. Oxygen by mask with a rebreathing bag (which has to be filled at all times) is given to all patients. If the patient objects to the mask, a two pronged nasal cannula is used. Pain is treated with either Morphine sulphate or Demerol.

The beta stimulating Isoproterenol (Isuprel®) as a microdrip, 2 mg. in 500 cc. of 5% glucose in distilled water, is usually given first, to achieve a systolic pressure of 90-100 mm. Hg., warm skin and urine excretion. If Isoproterenol fails, Metaraminol (Aramine®) 100 mg. in 500 cc. of 5% glucose in distilled water is given. Levarterenol (Levofed®) 4 mg. in 500 cc. is used only rarely, when the other drugs fail. We add large doses of steroids at times (Decadron® or Solucortef⁰ or Solumedrol®) to the intravenous infusion but no definite conclusion could be reached about their effect in preventing fatalities. Plasma transfusions or 6% Dextran in saline is used if a low central venous pressure indicates hypovolemia in the presence of shock.

Heart failure is treated early in every patient. The nurses are taught to recognize engorged neck veins, persistent basal rales, apical third sound and cough. Portable chest films may be the first clue of beginning heart failure. If heart failure is diagnosed the patient is digitalized as previously described and oxygen either by mask or cannula is given. If pulmonary edema develops intermittent positive pressure with 60% alcohol is used. Diuretics such as 1½ cc. Mercuhydrin or Thiomerin is given subcutaneously or Hydrochlorothiazide, Furosemide, or Ethacrynic acid are used orally. In fulminant pulmonary edema 25 to 50 mg. Ethacrynic acid (Edecrin®) intravenously was helpful at times. An automatic rotating tourniquet machine is used if necessary and if the patient is not in shock, sitting up in a comforable chair has at times resulted in improvement.

To prevent pulmonary emboli the nurses and house staff are instructed to examine carefully the patient's legs daily for calf and medial thigh tenderness, shinbone tapping tenderness, and Homan's sign. If thrombophlebitis is found, intravenous Heparin usually 5000-7500 units is given in divided doses q. 4 hours to increase the clotting time to at least 2½-3 times of normal. In patients with contraindication for Heparin, we have used daily 6% Dextran in saline infusions giving 40 drops a minute for 4-5 days. Development of chest pressure or retrosternal burning, dyspnea and rash are indications for discontinuing this infusion immediately.

Anticoagulation is not routine for every patient with myocardial infarction in the Unit.

Cardiac arrest did occur in our Unit. All accepted measures of cardiac resuscitation were promptly employed, usually first by the nurse. Cardiac arrest may be expected as the terminal event of a failing myocardium. In unexpected cardiac arrest, resuscitation was usually successful. Where it was unsuccessful, autopsy reports often revealed either a perforated septum or ruptured ventricle, incompatible with life. In expected arrests, it was also possible to restore a rhythm compatible with life, but the heart muscle was not strong enough to maintain successful circulation and the patient eventually died. If cardiac arrest occurred due to ventricular fibrillation the patient was immediately defibrillated without any other resuscitation measures and at times the patient regained consciousness shortly after defibrillation. Ample sodium bicarbonate, Lidocaine and, if necessary, Isuprel by infusion, is given after defibrillation.

If cardiac arrest developed before a monitor could be attached the chest was pounded and then, if needed, a countershock of 400 Watt/seconds direct current was used immediately. No harm is done if subsequent monitoring showed the cardiac arrest was due to ventricular standstill. If defibrillation failed to restore successful heart action and respiration, mechanical resuscitation with artificial respiration was started immediately. Patients once successfully resuscitated were kept under special supervision and for a longer time in the Unit, since without aggressive preventive treatment, the fatal arrhythmia tends to recur.

Discussion

Based on our experience it would be desirable to prolong the stay in the Unit to at least one week, and, for patients with recurrent major arrhythmias, even longer, until the arrhythmias have disappeared completely for several days. Perhaps a longer period of time might have prevented some deaths (Figure 2.) Therefore, while an average stay of four days was adequate for most patients, a Unit of 6 to 8 beds would be more desirable for an admission load of 298 patients yearly.

Successful resuscitation per se probably does not alone explain the marked decrease in the mortality rate. Patients previously often died unexpectedly because premonitory signs and symptoms of sudden death were undetected. We believe the decrease in mortality rate was mostly due to early recognition and prevention of life-threatening arrhythmias by aggressive treatment, in agreement with results reported by others.[5]

It is our impression that prophylactic use of Quinidine or Pronestyl in proper dosage will reduce fatalities from acute myocardial infarction. This is presently the subject of a cooperative study involving St. Raphael's and four other medical centers in the United States. Further accumulation of data in these hospitals will substantiate or repudiate this impression.

If the desired purpose of the Coronary Care Unit is to save lives, to continue research, to rather prevent life-threatening complications than to treat them, and to achieve this result with the greatest economy of personnel and apparatus, the Coronary Care Unit at the Hospital of St. Raphael's and its adjacent special nursing unit was successful as judged by the decrease in deaths during the first four days in the Unit and during the ensuing seventeen days in the special nursing unit.

Summary And Conclusion

Of 596 patients with suspected acute myocardial infarction admitted to a four-bed Coronary Care Unit of St. Raphael's Hospital during the last two years, 369 were proven by electrocardiograph and enzyme changes. Of these, 15.2% (57 of the 369 patients) died during hospitalization. In the year before the existence of the Coronary Care Unit, 27% (55 out of 202 patients) died (Figure 3). The mortality rate of patients treated prophylactically with Quinidine or Pronestyl according to a cooperative research protocol seemed to be even further lowered. (5.5% mortality rate with Pronestyl prophylaxis, 4.1% with Quinidine prophylaxis, 13.8% without any prophylactic antiarrhythmic drug in a total of 161 studied patients).

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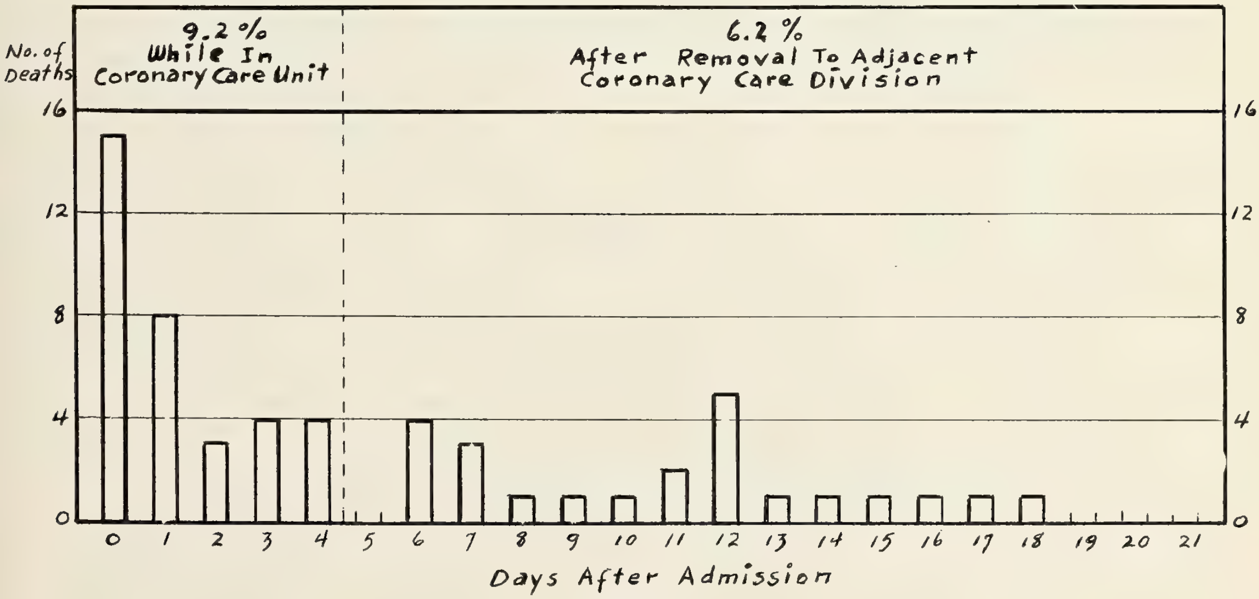

FIGURE II

Number of deaths of live admissions with proven myocardial infarction by number of days after admission.

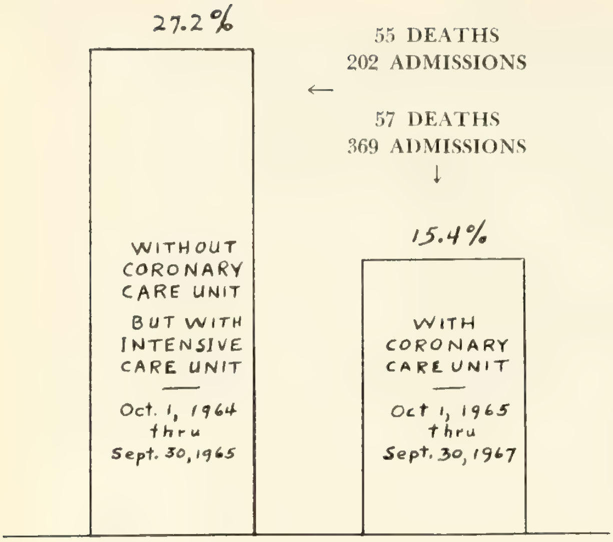

FIGURE III

Percent deaths of live admissions with proven myocardial infarction.

Abington (Pa) Memorial Hospital; Lawrence E. Meltzer, MD, Presbyterian Hospital, Philadelphia; William H. Rosenblatt, MD, University of Mississippi Hospital, Jackson; Oscar Roth, MD, Hospital of St. Raphael, New Haven, Conn. *Coordinators*: Jacob E. Bearman, PhD, and Byron W. Brown, Jr., PhD, University of Minnesota, Minneapolis (Statistical); George H. Berryman, MD, PhD, University of Illinois, Chicago, and Abbott Laboratories, North Chicago, Ill. (medical).

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Acknowledgment

We appreciate deeply the full cooperation of our colleagues on the staff, the encouragement and help given by Sister Louise Anthony, administrator, Dr. Donald Dock, Dr. John Christoforo, and Mrs. Daine Brown, M.S.N. and of Lorraine Gersz R.N., Jean Lukas R.N., Carol Brinkman R.N., Anne Williams R.N. and Jane MacMillan R.N. whose skill and devotion made this study possible. We also acknowledge the help of Dr. Philip Bondy, Dr. Louis H. Nahum, Dr. George Berryman, Dr. Morris Seide, Goodwin Wolff, and Mrs. Rene Kra for their valuable suggestions in writing this report.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

LOUIS H. NAHUM, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

THE PRESIDENT'S PAGE

Everybody wants good health care—and should have it. We physicians are the first to agree. In fact this is our *raison d'être.*

No one will deny that scientific advancements, both clinical and in the research laboratory, have increased dramatically our armamentarium for achieving this goal. The pharmacies overflow with miracle drugs, some permanent, some transitory. The engineers are introducing complicated electronic and other sensitive equipment. The tools are there, but what about the carpenters?

What is this man-power problem in the medical field that is on every planner's lips? And where do we find the solution to it? It is evident that the physicians must astutely interpret these highly technical tests and then select and direct the appropriate means of treatment. But he cannot do all this single-handed and still be efficient in the use of his capabilities.

John W. Garner, M.D., recent Secretary of Health, Education and Welfare, urges us to consider the coming "crunch" between the virtually limitless expectations of the American people for social benefits and the markedly limited resources for delivery. "Intelligent use of limited resources requires orderly formulation of goals, evaluation of means to achieve those goals, and development of strategies for getting from where we are to where we want to be." Through the Comprehensive Health Planning Act (P.L. 89-749), the Regional Medical Program (P.L. 89-239) and various voluntary agencies we should discover where we are. Unless the temptation of free-flowing government grants stimulates premature action, a proper goal can be established and vigorously pursued.

While infinite detail is yet to be delineated by the planners, we might well examine three factors: training, interest and compensation. Today a team approach to patient care is vital, with the amount and type of training for each team member adjusted to his duties and responsibilities. The short supply of nurses can be corrected only if more nurses are trained to teach them. Yet if all nurses are trained to teach or be administrators, who will take care of patients? A Master of Science or even Bachelor degree is not necessary for a good practicing nurse. Such a requirement takes too much time and expense, and would eliminate many able candidates. The training of nurses in the community hospital "diploma schools," so vital to our present supply, must continue a long time despite attempts to abolish them. A variety of programs must prepare the various technicians and aides, perhaps with new categories to be added.

Exposure to instruction does not necessarily guarantee interest. People are people and they want to be considered as such, not as a punch-card or a piece of machinery that needs to be kicked to make it run. They must have, and be helped to have, a sense of self-importance and pride in themselves and in their accomplishments. On the other hand, the team must have only one boss—and the urge for authority is great, greater than for responsibility.

Industry is employing more handicapped workers, as medicine has long done. A challenge is presented to them. The satisfaction of meeting that challenge, of being contributory, maintains interest and builds self-esteem, so they do even better. When the challenge to some one is too great, frustration results. A staff nurse, unhappy at not being able to do all she would like to for all her patients, may resign, thus putting part of her load on the other over-burdened nurses. Also the individual whose capacity and talents are not put to the test may do far less even than the little that is required. In the medical field generally the urge has been and still is to deliver quality.

In these days of strikes for more pay and shorter working hours, when the unskilled, untrained, inexperienced worker receives higher wages than a college graduate, it is not surprising that the number of engineering students is diminishing—and that recruitment in the medical and allied health care fields is tedious and not overly rewarding. Years of training at self-expense and other years at minimal pay are quickly lost to the memory of those who advocate more money for less work and more medical care for less money. They can't continue to have champagne and caviar at the price of beer and pretzels.

E. Tremain Bradley, M.D.

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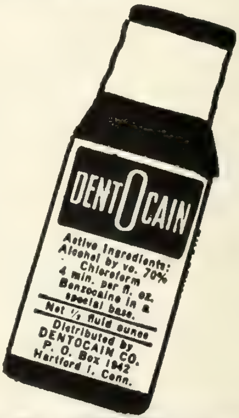
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CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1968 Annual Meeting of the House of Delegates will be held in the Terrace Room of the Hartford Hilton Hotel, Hartford. The first session of the House of Delegates will commence at 9:00 o'clock in the morning of Tuesday, April 30. Following luncheon, reference committee hearings will be held. The final session will commence at 3:30 o'clock in the afternoon of Wednesday, May 1.

E. Tremain Bradley, President
Kenneth F. Brandon, Speaker of the House
Charles Polivy, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider rsolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the Bylaws were presented to the House of Delegates on December 13, 1967 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

(PER DIRECTIVES OF HOUSE OF DELEGATES APRIL 25, 1967) PREPARED AND APPROVED BY THE COUNCIL

I. Committee on Publications

Purpose: To abolish the Committee on Publications

Amendment

ARTICLE XI—Divisional Boards and Committees
Section 3. Divisional Standing Committees
(D) Publications Division
Delete the words "Committee on Publications"
Section 5. Duties of Standing Committees
Par. 14 Committee on Publications
Delete the entire paragraph
Renumber the succeeding paragraphs appropriately

II. Committee on AMA-ERF

Purpose: To abolish the Committee on AMA-Education and Research Foundation

Amendment

ARTICLE XI—Divisional Boards and Committees
Section 3. Divisional Standing Committees
(A) Education and Hospitals Division
Delete the words "Connecticut Committee on American Medical Education Foundation" (now called Committee on AMA-ERF)
Section 5. Duties of Standing Committees
Par. 8 Connecticut Committee on American Medical Education Foundation (AMA-ERF)
Delete the entire paragraph
Renumber the succeeding paragraphs appropriately

III. Advisory Committee to State Commissioners of Welfare, Finance and Control

Purpose: To change the name of the committee to "Liaison Committee with the State Commissioner of Welfare"

Amendment

ARTICLE X—Committees of the Council

Section 3. Representatives and Advisors

Par. 1. Outline

On line 3, change to read: Liaison Committee with the State Commissioner of Welfare

Par. 4.

Delete entire paragraph and substitute therefore the following:

Par. 4. *Liaison Committee with the State Commissioner of Welfare*

The Council shall elect annually a Liaison Committee with the State Commissioner of Welfare, to consist of not less than five members and appoint the chairman thereof. The purpose of this Committee shall be to maintain continuing liaison with the commissioner of welfare, to foster and promote cooperative relations between the commissioner, employed state personnel and all members of the medical profession, and to make recommendations concerning all professional aspects of the medical care and hospitalization of the beneficiaries of state-operated medical assistance programs.

IV. Delegates to the Council of New England State Medical Societies

(*not* a directive of the House of Delegates)

Purpose: To conform with the new CNESMS bylaws, calling for six (6) delegates from each member organization, instead of the former three (3)

Amendment

ARTICLE X—Committees of the Council

Section 3. Representatives and Advisors

Par. 10. Delegates to the Council of New England State Medical Societies. Change the wording of the first sentence to read: "The Council shall elect annually six delegates to the Council of New England State Medical Societies and designate the chairman thereof." The balance of the paragraph will remain unaltered.

V. Committee on Postgraduate Education

(*not* a directive of the House of Delegates)

Purpose: To make it *not mandatory* that a Clinical Congress be arranged and conducted annually. This would not preclude the Committee on Postgraduate Education from conducting future Clinical Congresses, if it were felt desirable to do so.

Amendment

Article XI—Divisional Boards and Committees

Section 3—Duties of Standing Committees

Delete the underlined words in the following paragraph:

Par. 6. Committee on Postgraduate Education. The Council annually shall nominate to the House of Delegates a Committee on Postgraduate Education to consist of not less than seven members and nominate the chairman thereof. The function of the committee shall be to plan and make available programs of postgraduate education for members of The Society, *TO ARRANGE AND CONDUCT THE CLINICAL CONGRESS OF THE SOCIETY,* and to cooperate with university and other agencies within the state for the extension of postgraduate education of physicians.

Delegates To Annual Meeting

The Bylaws of the Society provide that each county association is entitled to one delegate in the House of Delegates for each thirty-five Active or Life Members in the association or fraction thereof based on the membership as of December 31st of the immediately preceding year. According to this, the quota of delegates from each county association who should attend the Annual Meeting of the House of Delegates which will be held in Hartford, April 30, 1968, May 1, 1968, and the Semi-Annual Meeting in December, 1968 is as follows:

County	*Membership Dec. 31, 1967*	*Official Delegates*
Fairfield	978	28
Hartford	1128	33
Litchfield	147	5
Middlesex	118	4
New Haven	1029	30
New London	212	7
Tolland	29	1
Windham	74	3

Election Of Councilors and Associate Councilors

Councilors and Associate Councilors, who shall serve for two years, shall be elected this year at the annual meeting of each of the county associations in Fairfield, Litchfield, New Haven and Tolland counties. In accordance with the Bylaws, each component association having over 750 members may elect one additional Associate Councilor. Therefore, the Fairfield and New Haven Medical Associations should elect a Councilor and two Associate Councilors for a two year term.

No Councilor or Associate Councilor elected by a component association shall serve more than three successive terms of two years each in his respective office, but after a lapse of one term of two years, such Councilor or Associate Councilor shall be eligible for reelection.

Newly elected Councilors and Associate Councilors shall not assume office until after the Annual Meeting of the House of Delegates.

SUMMARY OF ACTIONS
COUNCIL MEETING
Thursday, February 15, 1968

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Bradley, Gardner, Grendon, Polivy, Brandon, Caplan, Abbot, Fabro, Hess, Rogol, Cramer, Egan, Spitz, Ayres, Nolan, Jacobson, Jr., Johnson, Petrie, Pelz, Granoff and Roch. Also present: Mrs. Lindquist, Mr. Villano, Mr. Norbeck (AMA) and Dr. Richards. Absent were: Drs. Hastings, Shepard, Grant, Wilson and Palomba.

II. Routine Business

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Jane Lockwood, New Milford (FCMA)
Joseph Brandriss, Newington (HCMA)
Frank S. Vogel, Bristol (HCMA)
Howard L. Warring, Hartford (HCMA)
John C. White, New Britain (HCMA)
Louis E. Garston, Torrington (LCMA)
Luca E. H. Celentano, New Haven (NHCMA)
Margaret D. Craighill, Jamestown, R.I. (NHCMA)
Lewis C. Foster, New Haven (NHCMA)
Salvatore Liotta, Norwich (NLCMA)
John C. Raymer, Norwich (NLCMA)

CSMS Dues Exemptions

It was VOTED to grant exemptions from payments of CSMS membership dues to the following Active Members, for the reasons and periods indicated:

Joseph M. Corey, Norwalk (FCMA)—1968—Military duty
Samir E. Marrash, Bridgeport (FCMA)—1968—Military duty
Herman R. Schoenwald, Darien (FCMA)—1968—Residency training
David Steinberg, Stamford (FCMA)—1968—Military duty

Date of Next Meeting

The next meeting of the Council will be held on Wednesday, March 6, 1968, starting at 2:00 P.M.

III. Old, New and Special Business

Election of Student Members

It was VOTED to elect to Student Membership four applicants as follows:

Culley C. Carson, III, 48 Tobey Avenue, Windsor
George Washington University—1971
Pre-Med: Trinity College (Hartford)
Parent: Culley C. Carson, Jr.
Mark Leslie Engel, 42 Hollow Oak Lane, Stamford
State University of New York,
Downstate Medical School—1971
Pre-Med: Lafayette College
Parent: Bernard S. Engel
Stewart Alan Farber, 231 Logan Street, Bridgeport
University of Vermont—1971
Pre-Med: Brown University
Parent: Sam Farber
Edwin Gerhardt Singsen, RFD #2, Box 14, Storrs
University of Vermont—1971
Pre-Med: Ohio Wesleyan University
Parent: Edwin Pierce Singsen

Report—Committee on Preliminary Study of Nominations

After making a series of amendments to the report submitted by the Committee, it was VOTED to accept the report of the Committee and to transmit the amended report to the House of Delegates at its 1968 Annual Meeting as the official slate of nominees recommended by the Council. Nominations for CSMS officers to be elected in 1968 are:

President:
Norman H. Gardner, East Hampton (MCMA)
President-Elect:
Stevens J. Martin, Hartford (HCMA)
Vice-President:
Max Caplan, Meriden (NHCMA)
Secretary:
Charles Polivy, Hartford (HCMA)

Treasurer:
David A. Grendon, Sharon (LCMA)
Speaker of the House:
Kenneth F. Brandon, Hartford (HCMA)
Vive-Speaker:
Frank K. Abbot, Waterbury (NHCMA)
AMA Delegate:
Max Caplan, Meriden (NHCMA)
Alternate AMA Delegate:
Sidney L. Cramer, Hartford (HCMA)
AMA Delegate:
Orvan W. Hess, New Haven (NHCMA)
Alternate AMA Delegate:
E. Tremain Bradley, Norwalk (FCMA)
Councilor-at-Large:
E. Tremain Bradley, Norwalk (FCMA)

Reports—Council's Fiscal Advisory Committee

Four reports of the FAC were acted on as follows:

(a) *AMA Third National Congress on Health Education of the Public*: It was VOTED to approve the recommendation of the FAC that the PR Director, Peter F. Villano, attend this Congress (Chicago, April 4-6, 1968) as a representative of the Society, and that his usual expenses be paid by the Society.

(b) *Proposal—Committee on National Legislation*: It was VOTED to approve the recommendation of the FAC that up to $1500 be allocated to the budget of the Committee on National Legislation to cover the costs of a CSMS delegation of ten members going to Washington, D.C., April 3-4 to visit with Connecticut Representatives and Senators and to entertain them at a dinner, in accordance with a plan for same submitted by the Committee on National Legislation.

(c) *Annual Meeting Program on Medicine and Religion*: It was VOTED to approve the recommendation of the FAC that an additional $100 be allocated to the Committee on Medicine and Religion to cover the costs of this program, which, with the $750 previously allocated, makes the amount of the total funds allocated to the Committee for the program "up to $850".

(d) *Survey of Membership re Use of Out-of-State Laboratories*: It was VOTED to approve the recommendation of the FAC that up to $225 be allocated to the Committee on Public Health to conduct this survey, the project to be implemented via a questionnaire sent out as a supplement to the Journal. The questionnaire supplement will be self-sealing for returning to the CSMS office, will bear the return address on the reverse side, and will provide for post-paid return postage.

Report—Ad Hoc Committee on Workmen's Compensation Laws

Morris A. Granoff, New Haven, a member of the Ad Hoc Committee, reported that a study of the Workmen's Compensation statutes (including amendments enacted in 1967) revealed that the Compensation Commissioners now have considerable authority and responsibility to appoint physicians to, and to dismiss them from, approved panels of those eligible to treat compensation cases. It was VOTED to accept the Ad Hoc Committee's report and to approve recommendations as follows:

(a) That the President and the Chairman of the Council, in consultation, appoint an Advisory Committee to the Workmen's Compensation Commissioners, and that the Chief Compensation Commissioner be informed of the availability of the Advisory Committee to assist the Commissioners in appointment of qualified physicians to approved panels and in other matters related to the Workmen's Compensation program. One member of the Advisory Committee is to be a member of the Committee on Third Party Payments.

(b) That the Ad Hoc Committee be discharged, with thanks.

Presentation—Connecticut Regional Medical Program

Dr. Henry T. Clark, Jr., Program Coordinator of CRMP, joined the Council to make a comprehensive presentation of the work of the CRMP from its inception to date, and of several plans which have evolved from studies that will become operational in the near future. It was VOTED to thank Dr. Clark for his excellent presentation, and to invite him and members of the CRMP staff to join the Council again at a "special" meeting of the Council for the purpose of exploring in depth some of the matters which he was able to touch on at this meeting because of the limitations of time.

Presentation—CMS, Inc. re New "Century Contract"

Representing Connecticut Medical Service, Inc., Drs. William H. Horton, Willard E. Buckley, Elwood K. Jones and Richard Spillane and Mr. Howard Bierkan, joined the Council to explain the concepts and provisions of the new "Century Contract" in which CMS is now soliciting physician participation and which it hopes to offer for public sale in the near future. Following a question and answer period, the Chairman thanked the CMS representatives for appearing to make the presentation. Through extended discussion, a five-point evaluation of the Century Contract was developed and it was VOTED to inform the membership forthwith of this five-point evaluation.

Progress Report—Committee on Disaster Medical Care

It was VOTED to accept as information a report filed by John Shoukimas, Chairman of this Committee, ino response to an 8/3/67 inquiry of the Council concerning what plans the Committee is formulating to arrange and conduct a series of exercises in disaster medical care throughout the State as a function of the Society, using an HEW (USPHS) grant to the Society for this purpose. It was further VOTED to request Dr. Shoukimas to provide the Council with more specific information as to what role the Committee, itself, will play in this project, and to inform him that the Council's approval of engaging a dentist as "consultant" to the Committee and of a proposal to use CSMS grant funds to co-sponsor (with six other agencies) an April seminar on "emergencies associated with civil disturbances" will be contingent upon receiving this specific information from the Committee.

Communication—New Haven County Medical Association

The Council received notice that, on January 25, 1968, the membership of NHCMA voted to adopt a resolution concerning "third party contracts or indemnity arrangements with community hospitals" which said (in part) that "in the public interest, the personnel and facilities of every community hospital in Connecticut should be kept available on an equal footing to every person residing in the hospital's community area of service" and that "NHCMA expresses deep concern regarding proposals which would, by contract or indemnity arrangement, require the making of a preferential commitment of any portion of the personnel and facilities of any or all community hospitals in New Haven County to servicing patients enrolled in any particular type of insurance, prepayment, medical assistance or teaching and research plan, whether such a plan be private or public in nature". The NHCMA has forwarded copies of the resolution to the members of the Board of Directors and the Chief of the Medical Staff of all community hospitals operating within New Haven County, with the recommendation that no such preferential contract or indemnity arrangement be entered into by any of those hospitals.

The Council VOTED to endorse, with commendation, the NHCMA positions on the subject matters defined in the resolution. Since it was reported that the Yale-New Haven Medical Center has already been approached by the corporators of the New Haven Health Care Center Plan, seeking a contract or indemnity arrangement for the Plan's future subscribers (none are enrolled yet), it was further VOTED to notify the Board of Directors, the Dean of the Medical School and the Chief of the Medical Staff at the Yale-New Haven Medical Center of this action of the Council in support of the NHCMA resolution.

Pursuant to the foregoing, it was VOTED to invite the corporators of the Health Care Center Plan to meet with the Council at an early date to define the administrative policies and professional practices which the Plan intends to follow at such time as it is ready to begin operation.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on February 15, 1968. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

PLACEMENT WANTED

ALLERGIST—Board eligible internist with special interest in allergy wishes to locate in Connecticut. Connecticut license, presently completing military duty. Wishes to practice with a partner or in a group. Available about March 10, 1968.

G.P.—Applied for Connecticut license. Well trained in Anesthesiology and would like to practice with an associate or in a solo situation. Military obligations completed, available, March, 1968.

OBS-GYN—Board certified Ob-Gyn Fellow, age 32, University trained, military service recently completed. Seeks group or association practice.

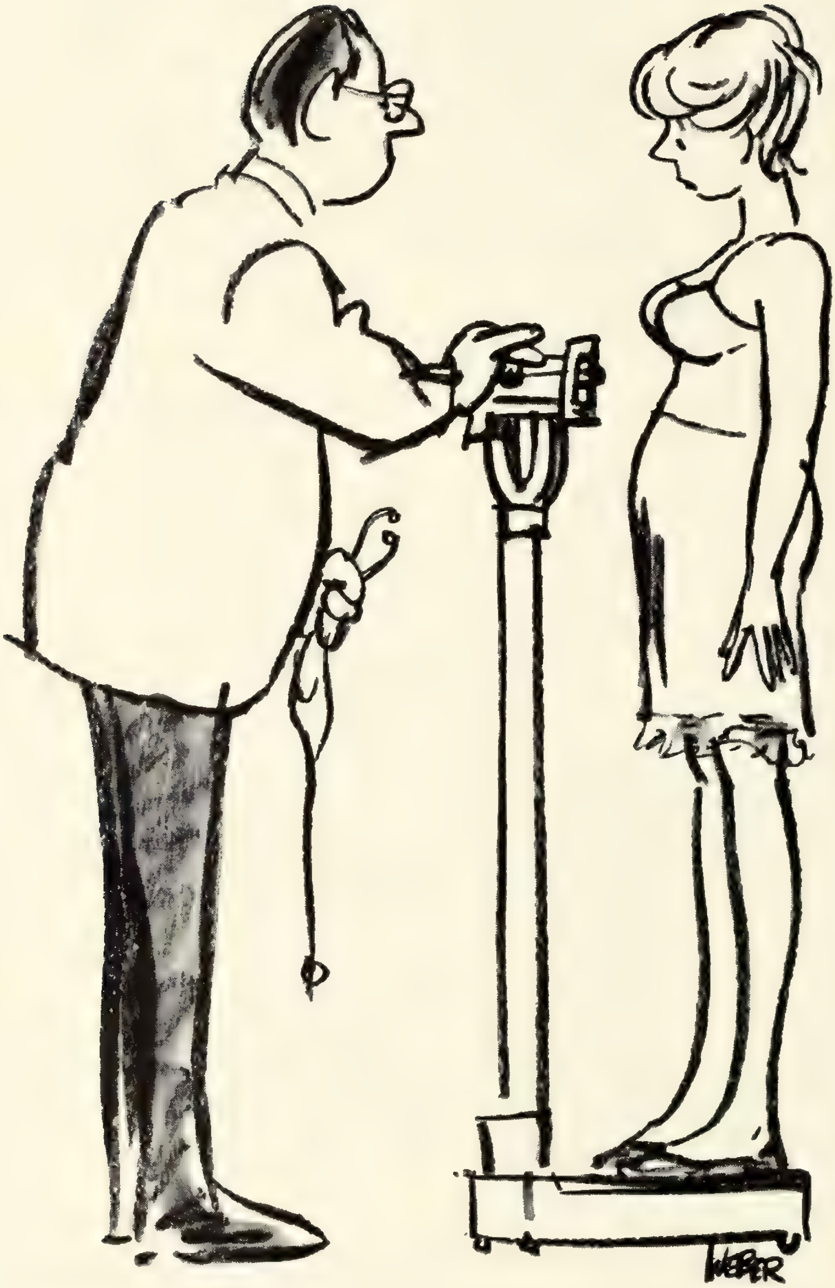
NEUROLOGIST—Board eligible, seeks clinical affiliation in Connecticut. Considerable experience in Internal Medicine, Neuropathology and Psychiatry. Connecticut license, military obligations satisfied.

PSYCHIATRIST—Board certified, 37 years of age, with extensive clinical and administrative experience, is interested in locating in Connecticut. Seeks (part-time) position in M.H. clinic or mental health center, in addition to private practice.

PLACEMENT OPPORTUNITIES

INTERNIST OR G.P. wanted in association leading to partnership with G.P. who has "quality" family practice. Do no surgery. Am associate attending at one hospital and courtesy staff at second. City of 175,000 in Connecticut. Phone 233-5554.

ESTABLISHED PEDIATRICS PRACTICE available. New owner to buy present owner's equip-



"You're up ten pounds since your last physical. We're going to have to do something about that."

Get them while they're easily reversible.

Obesity doesn't happen suddenly. This insidious process has its beginning—and the chances of reversing it are better—during the *first 10 to 15 pounds of weight gain.* When a new dietary pattern must be established, consider the adjunctive use of BAMADEX SEQUELS. Combining the proven *anorexigenic* action of d-amphetamine with the *tranquilizing* effect of meprobamate, BAMADEX SEQUELS controls appetite throughout the day, usually with a single capsule daily.

Contraindications: Dextro-amphetamine sulfate: In hyperexcitability and in agitated prepsychotic states. Previous allergic or idiosyncratic reactions to meprobamate.

Precautions: Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Bamadex® Sequels®

Dextro-amphetamine sulfate (15 mg.)
with Meprobamate (300 mg.)

Sustained Release Capsules

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LEDERLE LABORATORIES
A Division of American Cyanamid Company
Pearl River, New York

466-7

ment and share of office building. Terms of sale negotiable. Short distance from new medical school, excellent local hospital.

SENIOR STAFF PSYCHIATRIST, full time, residential psychiatric rehabilitation center 40 miles from New York in desirable living area with good schools. Non-profit organization oriented to intensive, individualized, eclectic psychotherapy. Large out-patient service also. Salary open, dependent on experience. Benefits include major medical insurance, life insurance and pension program. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

PHYSICIANS needed for full-time work at Masonic Home and Hospital, Wallingford, Connecticut. High salary, excellent benefits, good working atmosphere.

HOUSE PHYSICIAN—Diversified duties in voluntary, accredited hospital. Connecticut license required. 45 hours a week, Monday through Friday; no weekends. Immediate placement. Excellent salary. Write: P.O. Box 3474, Bridgeport, Connecticut 06604.

NEWLY APPROVED 3 YR. RESIDENCY now offered at Hartford Hospital with combined clinical experience at Newington Hospital for Crippled Children and the Gaylord Hospital. Teaching affiliation with Yale-New Haven Medical Center. Supervision under full-time psychiatrists. Experience available in a variety of child and adult disorders. Write: Carl V. Granger, M.D., Hartford Hospital CCU1, 80 Seymour Street, Hartford, Connecticut 06115.

WANTED: Internist, Board eligible, to associate with two busy young internists in modern spacious offices in a New Haven suburb. Excellent hospital facilities available. A fine opportunity for rapid growth. For further information contact: Marvin P. Zimmerman, M.D., or Edward S. Scherr, M.D., 960 Main Street, Branford, Connecticut 06405.

NEW YORK State Narcotic Addiction Control Commission has full or part-time openings to provide psychiatric services for resident addicts in rehabilitation centers in the Mid-Hudson River Valley area (Woodbourne, Beacon, Stormville, New York). Exceptional opportunity to supplement private practice in areas with minimal psychiatric coverage, or to begin long-range association with dynamic, challenging, total approach rehabilitation program. Bd. Cert. or Elgbl. Write Assistant Commissioner, S. Seymour Joseph, M.D., Dept. P-24, 1855 Broadway, New York, New York 10023.

FAMILY PRACTITIONERS (Internist or G.P.) Growing residential community of 12,00 in greater Bridgeport area has recently lost two family physicians and is desirous of obtaining at least two replacements. Hospitals nearby and staff appointments favorable. Fully equipped offices readily available for lease or purchase.

PSYCHIATRIST—Community oriented mental hospital. To work in or direct a 500-bed comprehensive mental health center, one of several units in a geographically decentralized 1600-bed hospital. Opportunity for teaching, clinical work and research. To work with or direct a team of social workers, psychiatric residents, psychologists, occupational therapists, and approximately 190 nursing staff personnel. O.P.D., day care, in-patient, consultation and emergency care available. Qualified candidates may be considered for other senior staff positions with starting salaries up to $23, 430. Opportunity for association with Wesleyan University, Yale University, and the University of Connecticut. Starting salary: $16,970. to $22,340. depending upon training and experience. Liberal fringe benefits. All particulars should be sent in first letter, including references. Write: Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

PSYCHIATRIC RESIDENCIES—available in a community oriented mental hospital. Comprehensive treatment facility for central Connecticut area. Associated with Yale University Departments of Psychiatry and Neurology which provides supervision and opportunities for training in areas of special interest. All Senior Administrators and Training Director Board Certified and on the faculty of Yale University. Special arrangements can be made for residents to be accepted for degrees in community mental health and hospital administration at the Yale School of Epidemiology and Public Health. Visiting lecturers. Seminars in transcultural psychiatry. Personal analysis can be easily arranged. Stipends: First year, $9050; Second year, $9530; Third year, $10,380. Liberal fringe benefits. Send all particulars with first letter to Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

ENDURON® | ENDURONYL®

METHYCLOTHIAZIDE

Each tablet contains
Methyclothiazide 5 mg. with
Deserpidine 0.25 mg. or 0.5 mg

Indications: Edema and mild to moderate hypertension (Enduron), and mild to moderately severe hypertension (Enduronyl). More potent agents, if added, can be given at reduced dosage.

Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™

Each tablet contains
Pargyline Hydrochloride 25 mg.
with Methyclothiazide 5 mg.

Indications: For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amendable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

TM-TRADEMARK

Contraindications: Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

Warnings: Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery ¼ to ⅕ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

Precautions: Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

Adverse Reactions: Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination.

801438

ABBOTT

MEETINGS

CANCER

May 8 1:30-5:00 p.m.

Management of Oral Cancer

Peters-Darrow Conference Room
Yale New Haven Medical Center
Registration Fee: $5.00

May 16 All Day

Quality of Survival of the Cancer Patient

Hotel America, Hartford

Sponsors: Connecticut Division, American Cancer Society; American College of Surgeons; Vocational Rehabilitation Branch, U.S. Department of Health, Education and Welfare

Description: Discussion of the problems of rehabilitation of the colostomy, mastectomy, and laryngectomy patient; discussion of the cosmetic defects resulting from head and neck surgery. Speakers, Milton Edgerton, M.D., Johns Hopkins; Richard Jessie, M.D. Anderson Hospital; Maus Stearns, M.D., Memorial Hospital of Cancer & Allied Disease; R. B. Turnbull, M.D., Cleveland Clinic Foundation. Registration at 9:00 a.m., medical sessions, 9:30-11:30 a.m. and 1:00-5:00 p.m.; dinner meeting at 7:30 p.m.

Registration (free of charge) limited by invitation to members of selected medical groups.

Contact: Paul G. Kuehn, M.D., 85 Jefferson Street, Hartford; Phone 524-5939

May 22 1:30-5:00 p.m.

Management of Laryngeal Cancer

Peters-Darrow Conference Room
Yale New Haven Medical Center
Registration Fee: $5.00

GENERAL

Hartford Hospital

Saturday Mornings 11:00 a.m.

March 30

Recent Development in Pediatric Cardiology

Speaker: James Manning, M.D., Professor of Pediatric Cardiology, University of Rochester Medical School

April 6

Steroids and Fever

Speaker: Philip Bondy, M.D., C.N.H. Long Professor of Medicine, Yale University School of Medicine, Physician-in-Chief, Yale-New Haven Medical Center

April 20

Individual Versus Population Normals

Speaker: Donald S. Yoong, M.D., Chief, Clinical Chemistry Laboratory, Clinical Center, National Institutes of Health

April 27

Aseptic Meningitis

Speaker: Martha Lepow, M.D., Associate Professor of Pediatrics, University of Connecticut School of Medicine

May 18

Compensatory Renal Hypertrophy

Speaker: Bernard Lytton, M.D., Professor of Urology, Yale University School of Medicine

May 25

Clinical Interprepation of the Pediatric Electroencephalogram

Speaker: Peter H. Berman, M.D., Department of Pediatric Neurology, New York University School of Medicine.

ANNUAL MEETINGS

March 28 3:30 p.m.

New Haven County Medical Association 184th Annual Meeting

Waverly Inn, Cheshire

April 9 4:30 p.m.

Fairfield County Medical Association 176th Annual Meeting

Frederick's, Fairfield

April 10 5:00 p.m.

Hartford County Medical Association 176th Annual Meeting

Hilton Hotel, Meeting

April 30, May 1-2

Connecticut State Medical Society 176th Annual Meeting

Hilton Hotel, Hartford

June 16-20

American Medical Association 117th Annual Convention

San Francisco

MEDICINE

March 27 9:30 a.m.-4:30 p.m.

Symposium on Thyroid Function Tests and Diseases

Manchester Memorial Hospital

Speakers: Herbert Selenkow, M.D., Assistant Professor of Medicine, Harvard Medical School; David Becker, M.D., Associate Professor of Medicine and Radiology, Cornell University Medical College; John Brooks, M.D., Assistant Clinical Professor of Surgery, Harvard Medical School; Bruce Bower, M.D., Clinical Endocrinologist, Hartford Hospital.

Open to all physicians Registration fee $2.00 including lunch

Contact: Martin Duke, M.D., Director of Medical Education, Manchester Memorial Hospital

April 10 9:00 a.m.-5:00 p.m.

Fourth Symposium of the Kidney Foundation of Connecticut

West Haven Veterans Hospital

Description: current concepts of the pathogenesis chronic pyelonephritis; clinical experience with the Giordano-Giovanette diet; recent findings in the immuno-pathology of acute and chronic renal disease; clinical management of the acidonic patient; clinical experience with the use of immuno-suppressive agents in the therapy of glomerculonephritis; clinical management of salt and water balance in chronic renal disease.

Registration Fee: $10.00, including a buffet luncheon

Program Co-ordinator: John Goffinet, M.D., Director of Hemodialysis, West Haven Veterans Hospital

Contact: Thomas Freeman, 357 Whitney Avenue, New Haven; Phone 777-1292

April 24 9:30-4:30 p.m.

Connecticut Conference on Prevention of Cardiovascular Disease

Stratford Motor Inn, Exit 53 Merritt Parkway

Sponsors: Connecticut Heart Association, Connecticut State Department of Health, Connecticut State Medical Society

Contact: Mrs. V. G. Schroeder Burham, Chairman 103 Shusted Lane, Greenwich

May 2-4

Fifth Annual Meeting of the American College of Clinical Pharmacology and Chemotherapy

Claridge Hotel, Atlantic City, New Jersey

No registration fee

May 9 10:00 a.m.

Tuberculosis Control and Eradication in Connecticut

Holiday Inn, Meriden

Sponsored by the Connecticut Thoracic Society and the Connecticut Tuberculosis and Health Association

Open to all physicians; no registration fee

Contact: Nicholas D. D'Esopo, M.D., West Haven Veterans Hospital; Phone 932-2561

May 15 All Day

Heart Diseases in Infants and Children

Yale-New Haven Medical Center

NATIONAL MEETINGS

April 1-5

American College of Physicians

Sheraton Hotel, Boston

April 15-20

American Physiological Society

Ambassador Hotel, Atlantic City

April 17-19

American Surgical Association

Sheraton Hotel, Boston

April 22-24

American Association for Thoracic Surgery

Hilton Hotel, Pittsburgh

April 22-27

American Academy of Neurology

Pick-Congress Hotel, Chicago

April 25-28

American Academy of Physical Medicine and Rehabilitation

Sheraton Hotel, Chicago

April 28-May 1

American Association of Plastic Surgeons

Shamrock-Hilton Hotel, Houston

May 1-2

American Pediatric Society

Seaside Hotel, Atlantic

May 5-6

American Society for Clinical Investigation

Chalfonte-Haddon Hall, Atlantic City

May 6-9

American College of Obstetricians and Gynecologists

Palmer House, Chicago

May 11

American College of Psychiatrists

Sheraton Hotel, Boston

May 15

American Society for Gastrointestinal Endoscopy

Bellevue-Stratford, Philadelphia

May 13-16

American Urological Association

Fontainebleau Hotel, Miami Beach

May 13-17

American Psychiatric Association

War Memorial Auditorium, Boston

May 15-18

Neurosurgical Society of America

Mark Hopkins, San Francisco

May 19-23

American Thoracic Society

Rice Hotel, Houston

May 27-29

American Ophthalmological Society

Homestead, Hot Springs, Virginia

Artists — Attention!

GENERAL INFORMATION: The Connecticut Physicians Art Association is planning the 1968 Art Exhibit in conjunction with the annual meeting of the Connecticut State Medical Society. At a recent meeting of this association, the following information is submitted for guidance to art hobbyists.

WHERE: Hartford Hilton Hotel, Hartford, Conn.

WHEN: April 30, May 1, 2, 1968.

ELIGIBILITY: Physicians (members of Connecticut State Medical Society) and their families are cordially invited to join this group of art hobbyists. (In the case of children and other members of physician's family, kindly indicate relationship to sponsor). All previous exhibitors are invited to show their works at this meeting and new exhibitors are cordially welcomed. Works eligible will include oil, water color, tempora, black and white and etchings, photography, pastels, collages, mixed media and sculpture. Paintings over 24 x 30 will be hung only at the discretion of the art committee depending upon available space.

JUDGING: Art works will be judged in four categories; 1. children under 16 yrs. (children over 16 yrs. will be judged with adults); 2. beginners; 3. intermediates; 4. professionals. Pictures should be framed and wired for hanging. The exhibit will be judged by professional artists.

COST: A hanging fee of one dollar ($1.00) will be charged for each entry and fifty cents ($.50) for children under 16 yrs. with two entries per artist. (Space equirements have caused our limiting the entries to two this year, as just noted.)

HOW TO APPLY: Entry blanks will be mailed to former exhibitors and also may be obtained by writing to the addresses of the committee listed below. One half of the entry blank should be be submitted to me at the below listed address with your check prior to April 15, 1968. The other half should be attached to the picture. Make checks payable to Connecticut Physicians Art Association. Please fill in entry blanks completely so that entry can be categorized easily in the above four noted divisions.

SUBMITTING: Art works must be submitted to a representative of the Art Association in the lobby of the Hartford Hilton Hotel on Sunday, April 28th, between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. It may be possible to aid exhibitors with the transportation of art works by contacting members of the committee noted below. These art works must be picked up on Thursday, May 2, between 12 and 4 P.M. Members of the art committee or their representatives will be in attendance at the display throughout the exhibit at the state meeting. The Connecticut State Medical Society (nor the Art Association) can assume no responsibility for loss or damage of any cause to art works.

If further information is needed, the following persons may be contacted:

Stewart J. Petrie, M.D. President, 56 Minerva St., Derby, Conn.; Mrs. Orvan Hess, Vice President, 29 Old Orchard Rd., North Haven, Conn.; Edward Williams, M.D., 269 Church St., Naugatuck, Conn.; Charles O'Neill, M.D., 18 Asylum St., Hartford, Conn.; Herman Austrian, M.D., 935 White Plains Rd., Trumbull, Conn.; Donald Morrison, M.D., 26 Birch Rd., West Hartford, Conn.; Eugene Rightmyer, M.D., 114 Sherman Ave., New Haven, Conn.; Mrs. Jonathan Shoukimas, Chairman Art Committee Woman's Auxiliary; C.S.M.S., 26 Pheasant Hill Dr., West Hartford, Conn.

Artists — Attention!

Under no condition can art work be accepted after April 28th.

Other auxiliary members may be contacted if further information is needed:

Hartford County —

Mrs. Donald Morrison, 26 Birch Rd., West Hartford; Mrs. Merrill Rubinow, 68 Butternut Rd., Manchester

Middlesex County —

Mrs. Clarence Harwood, 1350 Old Mill Rd., Middletown

Windham County —

Mrs. Ralph Gilman, Willow Brook Rd., Storrs

New Haven County —

Mrs. Mark Hayes, 163 Ridgewood Ave., North Haven; Dr. John Hoffer, 153 Main St., Ansonia; Dr. James Mooney, 299 Seymour Ave., Derby

New London County —

Mrs. Clifford Wilson, 19 East Town St., Norwich; Mrs. James Harkins, 98 Case St., Norwichtown.

From the reports, comments and compliments received from the past years' shows, this seems to be a point of major interest of the annual meeting of the Connecticut State Medical Society. We therefore wish to thank the art hobbyists and encourage their continued participation in this exhibit.

Stewart J. Petrie, M.D., President
Connecticut Physicians Art Association

PLEASE MARK YOUR CALENDAR

176th CSMS ANNUAL MEETING

To Be Held At The

HARTFORD HILTON HOTEL

HARTFORD

April 30, May 1, 2, 1968

OBITUARY

Goodrich Truman Smith, M.D.
1883-1967

Dr. Smith, a former attending surgeon in otolaryngology in the Waterbury Hospital, died at his home in Middlebury on August 3, 1967, at the age of 83, of congestive heart failure.

Dr. Smith, a Mayflower descendent, was a native of Woodbury, Connecticut. He attended the local schools, then Cushing Academy from where he went to Yale University. He was graduated from Yale Medical School in the Class of 1908. After he interned in Bellevue Hospital, where he became senior resident, he entered private practice in New York City and served in clinics in the College of Physicians and Surgeons Hospitals. Early in World War I he joined the Fordham Hospital Unit in the A. E. F. and was with that unit until after the armistice. While in France he met his future wife, Amparito Farrar, who was entertaining the troops in France under the auspices of the Y.M.C.A. She sang the "Star Spangled Banner" in the Paris Opera House in the big celebration of Armistice Day.

After the war, Dr. Smith returned to practice in New York and was attending surgeon at the Manhattan Eye and Ear Hospital in Otology, visiting professor in Mastoid Surgery at Columbia University, and otolaryngologist at the Welfare Island and City Hospitals.

In 1926, he retired to his old home in Woodbury, but within a year he opened his office in Waterbury practicing in diseases of the eye, ear, nose, and throat. He was an attending surgeon in otolaryngology in Waterbury Hospital until his retirement in 1943, because of poor health. He moved to Florida, and during the War ran an Eye Clinic for Children sponsored by the Lions Club in Naples. He returned to Connecticut in 1955 and had been living in Middlebury.

Dr. Smith was a Fellow of the American College of Surgeons, a member of the Waterbury Medical Association, and the Audubon Medical Society of New York.

Dr. Smith was a meticulous surgeon and was noted for his mastoid surgery. He once remarked, "I may not be brilliant, but I can always be thorough." He was impatient with imperfection.

He was an ardent collector of Dr. Samuel Johnson, the 18th Century Literary Great, and spent over 40 years gathering his works. Dr. Smith was considered an expert on the life and works of the English lexicographer.

Athletics always appealed to him, baseball and football in school, tennis and golf in his later years. He once held the Waterbury City Golf Championship. While in New York he was a team physician to John McGraw's New York Giants and was a consultant to the New York Boxing Commission.

Goodrich was a dynamic individual, a great competitor, full of energy and ideas, loyal to his friends, and very much interested in young people. He made a real contribution to medicine in Waterbury and the Waterbury Hospital, and his passing will be mourned by his family and many friends.

John H. Foster, M.D.

In Memoriam

Carter, Gray—Greenwich; Johns Hopkins University School of Medicine, 1928. Doctor Carter was an internist, a member of the American Board of Internal Medicine, and Director of Medical Services at Greenwich Hospital. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Doctor Carter died February 7, at the age of 67.

Woll, Ephriam — Danbury; Creighton University School of Medicine, 1942. Dr. Woll was a nationally recognized pathologist and educator. He served as director of the Danbury Hospital Laboratory from 1957 to 1962, and in recent years served as a consultant and a member of the hospital pathology department. He also taught pathology at Harvard Medical School, the University of Vermont Medical School, the University of Cincinnati Medical School, and the Albert Einstein College of Medicine. Dr. Woll was a Diplomate of the National Board of Medical Examiners and of the American Board of Pathologic Anatomy. He was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Woll died January 22nd at the age of 56.

WOMAN'S AUXILIARY

President
Mrs. Anthony P. Cipriano, Hamden

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INTERNATIONAL HEALTH ACTIVITIES

Shortly after the Korean War, a television program about needy Korean orphans so moved Mrs. Irene Auberlin, a Detroit housewife, that she became determined to help them. She immediately began collecting clothing and cribs from friends and neighbors, doctors and hospitals, business and professional people—anywhere she could find them. Everyone answered her plea by giving her their unused and discarded supplies and equipment. The first shipment weighed 4,000 pounds and went to an orphanage in Inchon, Korea. Since then, from this small beginning by one individual, the total shipment has grown to thousands of tons of medical supplies shipped to over 80 countries. Thus began the World Medical Relief Program.

At the post convention meeting of the Board of Directors, 1961, it was voted that the president be empowered to set up a committee for "Study of International Philanthropic Interests". She appointed two members from the board and three non-board members to this committee. This committee reported to the 1962 convention that the program is a tangible way for doctors' wives to be of service to a world-wide community. Projects endorsed by the committee at that time were: 1. leprosy relief programs; 2. medical books; 3. supplies and medical instruments; 4. world medical relief; 5. international hospitality.

This has been a popular activity with all auxiliaries since its beginning, for the relief of human suffering is a language all people understand, and we feel that it is a tangible way of expressing our friendship and good neighbor attitude. All the original five points as set forth by the planning committee have been carried out each year by the collecting of sample drugs, medical instruments, bandage material, hospital gowns from old shirts, leper bandages knitted, old eye-glasses, used medical textbooks and medical journals, X-ray equipment, office furniture etc.

These needed supplies are shipped to a hospital in Laos, a nurse in Cambodia, a doctore in the Philippines, a mission in Burma and over 300 medical missionaries in more than 80 countries. Hospitals, doctors and dentists have given drugs and equipment. Drug manufacturers have given pharmaceuticals. Volunteers, under the direction of registered pharmacists and nurses, have given countless hours for packaging. Trucking companies have given cross country transportation. And International Cooperation Administration, individuals, businesses or missions have paid the overseas shipping charges. All supplies must be used for and/or distributed free of charge to indigent patients.

The collected medical supplies are sent to World Medical Relief, Inc., and Direct Relief Foundation.

Medical and surgical supplies are sent to Catholic Medical Mission Board and Medical Assistance Programs, Inc. of Christian Medical Society.

Medical text books are sent to the Catholic Medical Mission Board, Christian Medical Council for Overseas Work, Medical Assistance Program, Inc. of Christian Medical Society and Darien Book Aid Plan.

Used medical journals sent to the "Doctor to Doctor Program—World Medical Association."

The auxiliary initiated a Vietnamese Student Aid Project, in support of the A.M.A. Vietnam volunteer projects, which partially supports graduate students in this country. These students will receive short-term specialized medical training and return to their country to teach.

Mental Health

Mental illness is the greatest public health problem of our time. If we are to live up to our ideal of service we must be prepared to lead the way toward better mental health and cooperate with others

in moderate hypertension and
poorly controlled mild hypertension
(when diuretics or sedatives are inadequate, for example)

When your patients expect a lot...

like relief from hypertensive symptoms
(headache, fatigue, nervousness, palpitation or insomnia, for example)

like an up-to-date, once-a-day dosage schedule
(a schedule not unlike timed-release medication, for example)

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(at 10¢ a tablet, for example)

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(as described in the package insert, for example)

...give them a little
(one tablet daily)

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chlorthalidone 50 mg., reserpine 0.25 mg.

Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Regroton should be used in pregnant patients or in women of childbearing potential only when, in the judgment of a physician, its use is deemed essential to the welfare of the patients; adverse reactions (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn.

Precautions: Antihypertensive therapy with Regroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue Regroton therapy two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Regroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angiitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. (B) 46-600-B

For details, see complete Prescribing Information.

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whose aims are similiar to our own. Auxiliary members are most fortunate in having several avenues open to them to help in the effort to control this problem.

1. Self education—Mental health begins with the individual, and we must practice the principles of sound mental health in order to be mature adults who can influence others through literature, films, lectures, etc.

2. Prevention—It is cheaper and less painful to prevent mental illness than to correct problems after they exist. Auxiliary members can cooperate with existing groups such as mental health associations, PTA's, church, etc., in working with young people, giving instruction, disseminating information and giving active leadership.

3. Community Service—Members should investigate facilities and participate in their activities wherever possible.

4. Volunteer Services—The value of volunteer services is no longer open to question. Auxiliary members should actively participate in the work of mental health clinics, half-way houses, rehabilitation centers, sheltered workshops, mental hospitals or psychiatric wards of general hospitals.

5. Recruitment—Auxiliary members, with an already existing recruitment program, should emphasize the need for capable personnel in all levels of mental health work.

6. Research—Auxiliary members can assist in research, primarily by donating funds.

7. Legislation—Auxiliary members are advised to be cognizant of legislation as it relates to mental health, and other activities in planning for community mental health centers.

The mental health "package program", "Timely Attention to the Mental Health of Children", depicts early tendencies toward maladjusted thinking and acting first grade children, and suggests remedial actions before these tendencies become symptoms of mental illness and necessitate treatment.

Among other educational programs available are a series of records for radio broadcasts entitled "Mirror to the Mind." "Milestones to Maturity" and "Milestones to Marriage" are a series of letters for use by controlled discussion groups of youngsters of junior high and high school age.

The suicide prevention program was initiated in 1963, because there are 20,000 known suicides a year with at least 100,000 known attempts a year, and suicide ranks 9th as a leading cause of death in the United States. The auxiliary function has been primarily educational. The showing of the film "Cry for Help" to police departments has helped them in the handling and recognition of suicidal individuals. Suicide Prevention centers have been established. This program has become one of our major efforts and a very effective program, well received and appreciated.

This problem of mental illness is not the misfortune of a few individuals or a few families. The problem, in one way or another, affects everyone, and only united efforts will produce substantial progress.

These are the last two of our orientation programs for the Auxiliary.

From Woman's Auxiliary A.M.A.
Member Orientation Manual
Mrs. Clarence Harwood

Around The State

NEW HAVEN COUNTY

Subject: Third Party Contracts or Indemnity Arrangements With Community Hospitals

WHEREAS: By definition, a community hospital receives support from the community in which it operates and, in turn, makes its services available to all community residents who need and seek them; and

WHEREAS: Special Act. No. 335, passed by the 1967 Connecticut General Assembly, authorizes a "Community Health Care Center Plan" based in the New Haven area to provide health care to its subscribers and engage in teaching and research, using such subscribers, through several different mechanisms, one of which is "by contract or indemnity arrangements with any hospital"; and

WHEREAS: Before the board of directors of the Community Health Care Center Plan has been formed to transact business for the corporation, and before any policies of the Plan have been made known to the general public, it is reliably reported that the Plan's Corporators are presently seeking to enter into such contracts or indemnity arrangements with one or more community hospitals in the New Haven area; and

WHEREAS: No other medical care and/or insurance or prepayment plan in Connecticut, public or private, is known to have sought from, or been granted by, any community hospital any special agreement that commits any portion of the hospital's personnel and facilities to specifically serving the subscribers of a particular plan; therefore be it

RESOLVED: That the New Haven County Medical Association express its conviction that, in the public interest, the personnel and facilities of every community hospital in Connecticut should be kept available on an equal footing to every person residing in the hospital's community area of service, without regard to the type of insurance, prepayment, medical assistance or other plan in which he may be enrolled; and be it further

RESOLVED: That the New Haven County Medical Association express deep concern regarding proposals which would, by contract or indemnity agreement, require the making of a preferential commitment of any portion of the personnel and facilities of any or all community hospitals in New Haven County to servicing patients enrolled in any particular type of insurance, prepayment, medical assistance or teaching and research plan, whether such plan be private or public in nature; and be it further

RESOLVED: That notice of these resolves be transmitted to the chairman of the Board of directors and the chief of the medical staff of all community hospitals operating within New Haven County, with the recommendation that, in order to protect the rightful interests of the general public, no contract or indemnity arrangement be entered into by a community hospital which would require the commitment of any portion of its personnel and facilities to servicing subscribers enrolled in any particular insurance, prepayment, medical assistance, teaching and research, or other plan of similar or related nature; and be it further

RESOLVED: That notice of these resolves be transmitted to the Council of the Connecticut State Medical Society as information, and for whatever action at state level may be deemed to be appropriate.

These resolutions were adopted at a Special Meeting of the New Haven County Medical Association on January 25, 1968 in the auditorium of the New Haven Medical Association Building, 362 Whitney Avenue.

H. A. Levin, M.D., *Clerk*

BOOK REVIEWS

PATHOLOGIC PHYSIOLOGY: MECHANISMS OF DISEASE. 4th Edition. Edited by William A. Sodeman and William A. Sodeman, Jr. W. B. Saunders Company, Philadelphia and London, May 12, 1967. 1051 pages. Illustrated, 30 Contributors. $19.00.

Reviewed by: LOUIS H. NAHUM

Students beginning their study of clinical science need a useful reference book and physicians need to refresh their knowledge of disease mechanisms. This book in its 4th edition after a lapse of six years will fulfill both of these needs. Since knowledge is advancing at a very rapid rate with obsolescence equally rapid, the editors and contributors have been confronted with a large task of sorting out and interrelating the mass of newer knowledge in a meaningful way. To the previous edition two new chapters have been added, one by W. A. Sodeman, Jr. on sub-cellular biology and pathologic physiology and the other by Sir F. M. Burnet on auto immune disease. But one can see extension of the molecular and chemical nature of disease throughout the book obviously inspired by the young Sodeman in his introductory chapter. In every chapter the attempt has been made to reach deeper into sub-cellular mechanisms and to promote a greater understanding of how and why symptoms appear.

There is much admirable material in this book. The chapter on disorders of blood and blood forming organs by W. B. Castle is charming, lucid and scholarly. Thorough revisions are in evidence in the chapters on infectious diseases with a reduction of data to basic concepts in mechanisms of disease. The chapter on the spleen and reticulo endothelial system has been entirely redone by Jandl and is reminiscent of Castle's masterpiece.

The chapter on the liver by Ingelfinger is of a high order. The one on the electrocardiogram by F. D. Johnston is quite well done but conventional. Many contributors have done a creditable job with some unevenness in quality as is to be expected in any ambitious multi-authored textbook.

By focusing on mechanisms of disease we obtain a book clinically oriented in which basic physiology and clinical medicine are fused into mechanisms of disease. It is, therefore, more than one finds in physiology texts and somewhat less than what one reads in text-books of medicine. It is a first class bridge between the two and is certainly one that will enrich the student and physician to the end of making better understood the way in which disease manifests itself dynamically. Just how treatment of heart failure found its way in this book is not easy to understand but it was done well nevertheless by Brachfeld and La Due.

THE HUMAN ADRENAL CORTEX: ITS FUNCTION THROUGHOUT LIFE: Ciba Foundation Study Group No. 27. Edited by G. E. W. Wolstenholme and Ruth Porter. Little, Brown and Company, 1967. 146 pp. with 26 illustrations.

Reviewed by: GEORGE L. COHN

It is most fortunate that Professor F. Verzár reached his eightieth birthday, because a conference was held in his honor on September 14, 1966, at the home of the CIBA Foundation in London, England. At that time, Dr. L. J. Soffer and friends (a Study Group, No. 27) celebrated Professor F. Verzár's birthday by presenting and discussing *The Human Adrenal Cortex*. This monograph is the written testimonial of this event.

The book is organized with a warm introduction by the Chairman followed by Professor Verzár's review of his fifty-six years of research endeavors in the fields of endocrinology and metabolism. After that auspicious blowing out of the birthday candles, one is then lead breathlessly from the foetal period of adrenal cortical function, through childhood and adolescence, pregnancy, surgical stress, acute medical stress, chronic disease, and finally old age. After a general discussion by the participants, the conference is closed by Dr. L. J. Soffer, who hopes that there is another party in ten years.

The contents of each chapter are written and edited in a scholarly fashion with judicious use of references (authors) and the dates of publication. But also one has to be impressed with the high intellectual levels of the discussions which are well documented and a delight to read. The provocative nature of the group was evident. It was moderated by the leader in an expert manner.

It is difficult to find fault with this monograph. In fact, one wonders why it would be necessary to be critical. Finally, Mr. William Hill merits kudos for a beautifully organized index. *The Human Adrenal Cortex* is recommended reading for all "Students of Medicine."

It would be a thoughtful present to give an associate.

THE MIDWIFE AND THE WITCH: Edited by Thomas R. Forbes. Yale University Press, New Haven, Connecticut, 1966. 206 pp. 16 illustrations, $$.50.

Reviewed by: ORVAN W. HESS

This scholarly book by Thomas R. Forbes, Professor of Anatomy and Associate Dean of Yale University School of Medicine, provides a profusely documented source of evidence of the long, and often gruelling, efforts required in the search of truth. Of high literary calibre, it is a most interesting and thought-provoking resume of selected subjects related to Medicine in which superstition has played a particularly prominent role. The treatise suggests that superstitions resulting from inferences based often on false premises have, on occasion, offered clues for solving the riddles concerning many reproductive phenomena.

In a pleasantly readable manner, Dr. Forbes has presented a review of a vast amount of material selected from a wide range of more than 900 sources. He has traced, with appropriate and significant personal observations, the origin, scope and development of midwifery over the centuries. The recognition for the need of proper training, close supervision of the practitioner, and elimination of the element of witch craft is noted in the description of the efforts of the church and state (Germany 1452) to regulate the cult of midwifery.

The book contains several unique illustrations of exceptional quality and medical interest. The extensive bibliography of more than 20 pages offers a particularly valuable source of reference.

This book is highly recommended to all as exceedingly interesting reading matter and as an account of the slow replacement of superstition, or popular notions, by scientific knowledge during the past centuries to be contrasted with the accelerated pace during the present era.

DIGITALIS THERAPY: A REAPPRAISAL OF DIGITALIS AND CARDIAC GLYCOSIDES. Edited by Alan F. Lyon and Arthur C. DeGraff. The C. V. Mosby Company, Saint Louis, 1967. 38 pp. $2.00.

Reviewed by: LOUIS H. NAHUM

This excellent monograph is a collection of articles which appeared in various issues of the *American Heart Journal* during 1966-1967.

This review shows the definite progress that is being made in our understanding of how digitalis acts. The older pharmacologic studies defined the now well-known isotropic and vagal actions of digitalis. The more recent research has explored the mechanism of action at the cellular level.

There is a developing field in which the chemical structure of the various glycosides relate to some extent to pharmacologic action. This, however, has not yet brought the basic research on digitalis and its clinical applications closer together. It is true that the availability of pure cardiac glycosides has indeed helped the physician, but there is great variation in dosage required from patient to patient and the narrow therapeutic range still pose real problems in using digitalis.

The articles in this booklet reveal that definite progress is being made and the physician who reads it will have a better grasp of the problems and pitfalls in the use of digitalis in heart failure.

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CONNECTICUT
STATE MEDICAL SOCIETY
Please Mark Your Calendar
176TH ANNUAL MEETING
April 30, May 1, 2, 1968
Hartford Hilton Hotel, Hartford
PLAN NOW TO ATTEND

Committee on Control of Infectious Diseases
American Academy of Pediatrics
INACTIVATED MEASLES VACCINE
Discontinuance of Use

In the past the Committee has listed among schedules recommended for measles immunization several which included inactivated (killed) measles virus vaccine.[1]

Unusual local and systemic reactions occurring when recipients of inactivated vaccine later encountered natural measles or received live attenuated measles virus vaccine have been documented in reports from the U.S.A. and elsewhere.[2-9] These reactions have taken two forms:

1. Exposure to measles has resulted in overt illness with an atypical rash (beginning on the feet and extending upward, concentrated on the lower extremities, with petechial, vesicular and urticarial components), pneumonia, edema, high fever and toxicity;
2. Administration of live vaccine has induced a reaction at the injection site with erythema, heat, tenderness, swelling and a localized vesicular or hemorrhagic lesion accompanied systemically by fever, malaise and regional lymphadenopathy.

All the variables which may affect the magnitude and incidence of these disturbing responses are not yet known. In one town, 11 of 66 children at risk developed the atypical illness when exposed to natural measles 4 years after administration of inactivated vaccine.[6] In a different setting, 9 of 31 children displayed local reactions when given live vaccine one year after a course of inactivated antigen.[5] Reactions of this sort have not been observed with live, attenuated virus vaccine or natural measles unless prior sensitization had been induced by the inactivated vaccine. Although the pathogenesis of these reactions has not been fully elucidated, their severity and frequency and the likelihood that less overt, unrecognized forms may occur, justify a reconsideration of the use of this vaccine at this time.

The Committee therefore recommends that:

1. Inactivated measles vaccine be deleted from all schedules of immunization.
2. Live attenuated virus vaccine be given as soon as possible to all children who may have received only inactivated vaccine previously and that their parents be cautioned of possible local and systemic reactions which may occur.
3. Children with underlying illnesses or receiving forms of therapy which contraindicate the use of live vaccines be given immune globulin (human) for protection on exposure to measles. Special attention should be directed to the prompt immunization of the siblings and close contacts of such children with live attenuated vaccine in order to reduce their opportunity for contact with natural disease.

References

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State Health Commissioner Warns About Diet Pills

Complaints and questions have been received by this department in recent months concerning use of multi-colored pills in weight reduction by certain physicians in Connecticut who have devoted a major part of their practice to weight reduction through use of these pills.

At least in some instances use of these medicaments is being enthusiastically promoted through symposia lasting 2 or 3 days put on by the pharmaceutical company at which time physicians, osteopaths and natureopaths employed for the occasion by the company are reported to extol the merits of this particular method of weight reduction above all others, minimizing the need for control of diet and according to at least one Connecticut physician who attended such a symposium promising rich rewards in the way of annual income for those who dispense the company's products for weight reduction in the "program" promoted by the company.

All or nearly all of this promotion appears to be by word-of-mouth. Even in conference with officers of the company in question I have been unable to obtain any printed materials claiming the combination of products promoted in symposia are useful in weight reduction or copies of any scientific reports of controlled studies comparing use of these products with other recognized methods of weight reduction.

The pills in question contain thyroid extract, digitalis, various vitamins and minerals, 2 or 3 male and female hormones, barbiturates, amphetamines and in some instances diuretics, iron and other substances.

Because of the great emphasis put on use of the pills, families of patients have reported patients under this regimen to have been given no advice concerning the need for either caloric intake or exercise with reference to reduction in obesity even in persons markedly obese.

Three deaths in Connecticut have occurred among persons on this weight reduction regimen. Two of the deaths might possibly be attributed to dizziness or momentary loss of consciousness resulting from some of the medication given. The other death was in a woman with diabetes who developed septicemia following surgery, and the practitioner treating the woman for obesity appeared not to have been treating her diabetes also.

It seems desirable to call to the attention of physicians in Connecticut through the medium of "Connecticut Medicine" the seriousness of the problem of using methods of obesity control which may be irrational and without scientific basis. At the same time the seriousness of treating properly diabetes and other conditions in persons with obesity should be recognized so as to avoid unnecessary mortality. County medical societies also might be helpful through their committees on ethics or professional conduct in reviewing questions coming to their attention concerning methods of treating obesity in their localities.

Franklin M. Foote, M.D., Commissioner

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Cellular Biology of the Uterus. Edited by Ralph M. Wynn. Appleton-Century-Crofts, New York, 1967. Division of Meredith Publishing Company. 524 pp. $22.50.

The Physiological Clock. Revised second edition. Edited by Professor Erwin Bünning. The Heidelberg Science Library, Volume I. Springer-Verlag New York Inc., 1967. 167 pp. with 126 figures. $3.00

Digitalis Therapy. Edited by Alan F. Lyon, M.D. and Arthur C. DeGraff, M.D. The C. V. Mosby Company, Saint Louis, 1967. 38 pp. $2.00.

Catecholamines in Cardiovascular Physiology and Disease. American Heart Association Monograph Number Seventeen. Edited by Dr. Ralph Reader. American Heart Association, Inc., 44 East 23rd Street, New York, New York, 10010. 247 pp. $3.00.

Symposium on Coronary Heart Disease. (Second Edition—Revised) American Heart Association Monograph Number Two. Edited by Herrman L. Blumgart, M.D. American Heart Association, Inc., 44 East 23rd Street, New York, New York, 10010. 161 pp. $3.00.

Vietnam Honors U.S. Physicians

Two U.S. physicians have been awarded the Vietnamese Medal of Honor for their voluntary service to the people of that war-torn country.

Alfred B. Swanson, MD, an orthopedic surgeon from Grand Rapids, Mich., has made four one-month tours to Vietnam since 1962 and has organized a hand surgery program through the Volunteer Physicians for Vietnam project of the American Medical Association.

Richard B. Stark, MD, a New York City plastic surgeon, is returning to Vietnam shortly for his fifth tour. He has organized a plastic surgery program. He and Dr. Swanson have always gone under the sponsorship of CARE-MERICO, paying their own way and all of their expenses.

Polio Campaign: Dr. Swanson pioneered in the development of a polio immunization program. He has worked in both military and civilian Vietnamese hospitals, repairing some of the many extremity wounds.' Much of his work has been with Vietnamese children.

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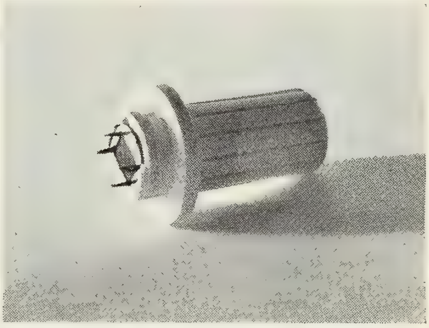

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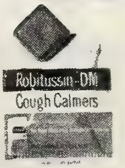

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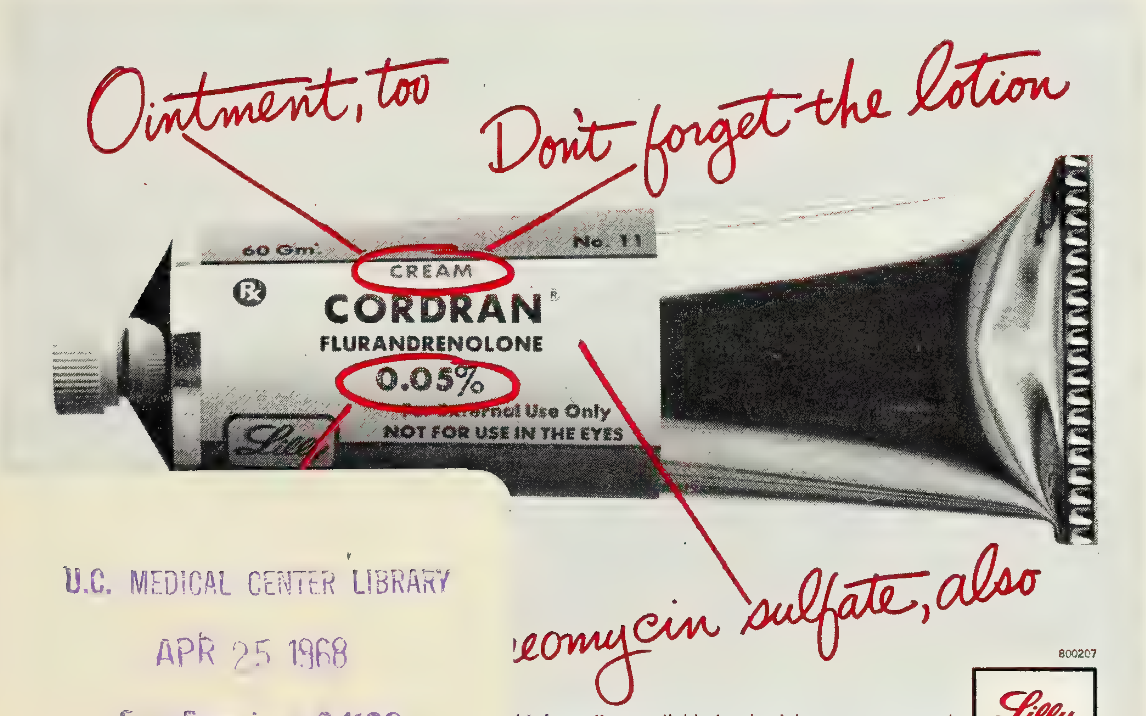

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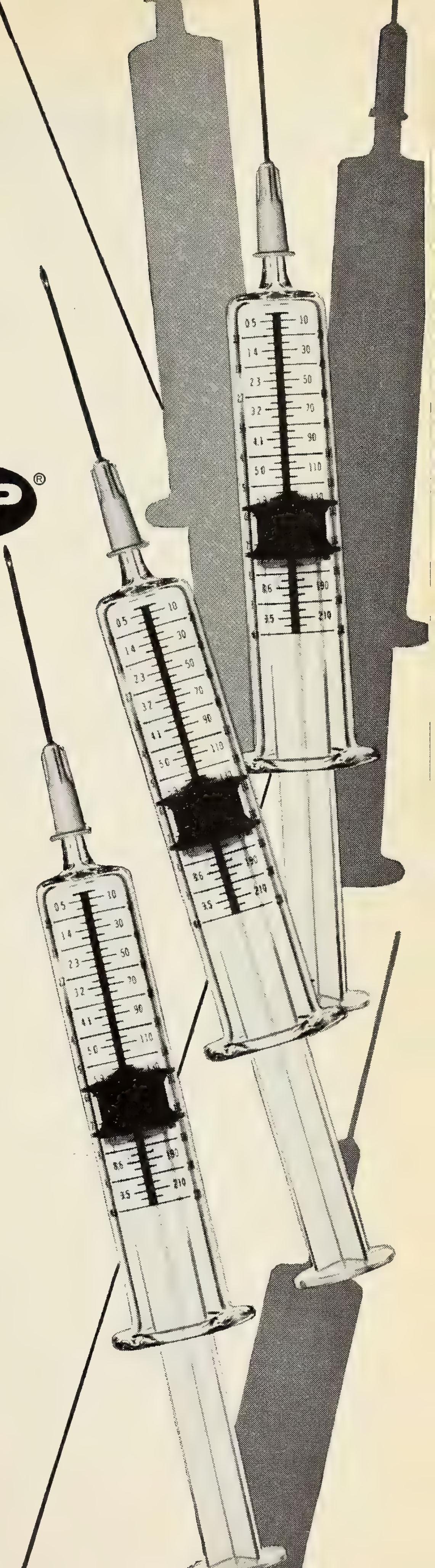

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Connecticut Medicine

editorials

Basic Science And Practical Medicine: Gastrin

It has been known since 1905[1] that an aqueous extract of gastric antral mucosa stimulates the secretion of acid and pepsin by the antral, not fundic portion of the stomach. Edkins named the substance gastrin presumably a contraction of gastric secretion. The original work did not clearly separate the effects of histamine from this substance. Finally, however, it became clear that besides histamine, the antrum truly secreted a protein-like substance that closely mimicked the action of histamine on gastric acid secretion. Thus it became clear that there is present an antral hormone mechanism for the stimulation of gastric acid secretion.

After Gregory and Tracy in 1961[2] developed a reliable method for the extraction of gastrin from hog stomach, there followed rapidly purification of two gastrins and total synthesis. Each gastrin exhibited the same physiologic properties although they were slightly different chemically. The gastrins of hog, dog, man and sheep are known to have closely related structures. Also that peptides composed solely of the 4N terminal amino acids of gastrin in the proper sequence have the same physiologic properties as those exhibited by the entire molecule. Gastrin unlike histamine can traverse the liver and not lose its action.

Now that we have a purified gastrin preparation to work with, we have learned that its action is not limited solely to gastric acid secretion. There have been uncovered a variety of other unexpected physiologic effects. It is an extremely strong stimulant of gastric acid secretion over five hundred times that of histamine. It is peculiar in that it inhibits gastric acid secretion when given in large doses. It causes increase in pepsin secretion even when acid secretion is inhibited. This finding, however, is present in the dog and not in man.[3] Gastrin also causes contraction of gastric and small bowel smooth muscle in dogs as well as on colon and ilium.[4] It also acts on postganglionic parasympathetic nerves to cause release of acetylcholine.

These manifold effects of gastrin extend to the pancreas and liver although large amounts are necessary to stimulate pancreatic enzymes.[5] [6] Obviously when we wish to put the pancreas at rest in acute pancreatic disease, it is important that we decompress the stomach by a gastric tube. In the liver gastrin increases water and bicarbonate output in hepatic bile. Gastrin also stimulates secretion of the intrinsic factor by the human stomach[7] in quantities twenty times as high as histamine. There are also inconsistent reports of the effect of this hormone on the circulatory system.[8] It is astonishing that this array of effects can be produced by a single purified hormone or its terminal tetrapeptide. However, we need to learn a lot more about the relative importance of the physiologic action of gastrin other than the stimulation of gastric acid secretion.

Numerous investigators have demonstrated that extracts of pancreatic tumors of the non-beta islet cells produce gastric acid secretory responses analogous to those of purified gastrin. These extracts also have the same effects on gastrointestinal mo-

THE COVER

CONQUERORS OF PAIN

BEFORE a skeptical group of surgeons in the operating amphitheatre of Massachusetts General Hospital, October 16, 1846, William T. G. Morton, Boston dentist, prepared to anesthetize Dr. John C. Warren's surgical patient, Gilbert Abbott, by causing him to inhale ether. Though Crawford W. Long, Georgia physician, had used ether for anesthesia in 1842, and Horace Wells, Connecticut dentist, tried unsuccessfully to demonstrate anesthesia with nitrous oxide in 1845, reports of painless operations resulting from Morton's methods gave practical anesthesia to mankind. Within a year, ether was being used in many hospitals world-wide to conquer pain incident to surgical operations.

tility and pancreatic secretion. They also have a high ulcerogenic potential (The Zollinger-Ellison Syndrome). Embryologically pancreatic islet cells arise from the same anlage as gastric antral cells and perhaps this is the reason why some cells destined to become antral cells might have become altered to develop subsequently into ulcerogenic pancreatic tumors. The existence of certain ulcerogenic tumors within the duodenal wall is consistent with this hypothesis. It is very possible that the substance liberated by the pancreatic tumors in the Zollinger-Ellison syndrome produce gastrin although so far the extraction and isolation of gastrin from these tumors remains to be accomplished.

The small intestine plays an important role in regulating and especially in inhibiting secretion of gastrin. Duodenal acidification definitely inhibits gastrin secretion in normal man as well as in patients with duodenal ulcer.[3] We are now permitted to draw important clinical inferences. They afford sound physiologic support for the preservation of normal duodenal contents in operations for duodenal contents in operations for duodenal ulcer. If we allow acid and fat into the small intestine, it should inhibit gastric acid secretion and therefore help to prevent recurrent ulceration. It is now better understood why massive resection of the small intestine especially of the ilium results in gastric hypersecretion in both animals and man for under such circumstances there is a loss of intestinal mediated inhibition. For the intestine to successfully inhibit gastric secretion it must contain fat in an absorbable form. Its absence after intestinal resection will therefore not play its necessary physiologic role in inhibiting gastric hypersecretion.

There are profound alterations that can be produced by vagotomy. In man it is followed by significant depression of the secretory effect of histamine and gastrin, whereas cholinergic drugs augment action of gastrin. Albe[9] clearly showed that without the antrum there is a marked reduction in acid secretory response to the stimulus of food and this response can be restored by subthreshold doses of gastrin. He also showed that a number of humoral agents derived from the small intestine can also potentiate markedly the response of the stomach to vagal stimulation. Apparently we may think of the vagus as a "priming device" in the regulation of gastric secretion.

It would appear that both the cephalic and gastric phases of gastric secretion are mediated by vasovagal cholinergic reflexes.[9] These can cause either direct cholinergic stimulation of the parietal cells or they can lead to release of antral gastrin. In this view gastrin is a "hormonal link in the neural chain." The enormous physiologic importance of the interaction of neural and humoral stimuli in the stomach is self-evident, although some new questions are raised: how important are cholinergic reflexes in the duodenal release of secretin or pancreozymin, what is the significance of the extra-gastric effects of gastrin?

The profound alterations produced by surgical vagotomy have come into focus but several questions remain. What is the merit of simple denervation of the antrum rather than its removal? What will be the long range effects in patients who have lost the stimulating effects of gastrin on the pancreas or liver? What would be the value of potent anesthetics taken by mouth with the aim of diminishing the release of antral gastrin, in non-operative therapy of duodenal ulcer? At any rate we now have an explanation as to why these operations that leave behind a stump of the stomach leave a propensity to develop new ulcers. A retained antrum is stimulated to produce gastrin by constant bathing in alkaline duodenal contents. Therefore, some of these patients develop hypersecretion similar to that in the Zollinger-Ellison syndrome.

It becomes clear why advances in our knowledge of gastric physiology within the past few years have been the most exciting and important in this area of interest in many decades.

L.H.N.

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Rational Therapeutics And Iatrogeny

Sir William Osler said that one of the first duties of the physician is to educate the masses not to take medicines and that we must remember how much we do not know. This was not therapeutic nihilism but rather a plea for therapeutic rationalism. For example when we use a drug such as amphenicol the physician must weigh the risk of the infection to the patient versus the risk of the drug to the patient. It is probably true that generally speaking physicians tend to overprescribe. In this year of "miracle" drugs patients more and more want medicines. When a patient is suffering from a "cold" or virus infection, every day of fever seems a threat to the patients health, they want an antibiotic to "quickly cure" his cold although we know it is useless and may even cause unwanted side effects. It is easier for the physician to yield to the patients demands than to educate the patient differently although this we must do.

We must do this on two counts, one when we must exercise restraint in the use of a drug contrary to the wishes of the patient, and the other when the drugs we use may induce diseases on their own account. For modern medicine has created an ever increasing group of artificially induced diseases. Originally Diseases of Medical Progress included iatrogenic disorders induced by autosuggestion based on the physicians mannerisms and discussions. The Heart Scare Syndrome is a good example.[1] But now the iatrogenic disease category has been expanded to include disorders from medication for diagnosis and from surgical procedures.[2-4]

Two recent events have focused our attention on the growing problems of iatrogenic diseases. The first was the thalidomide disaster of the early 1960's. The second was the report by Schimmel[5] that 20 per cent of hospitalized patients at a teaching institution experienced a deleterious complication directly related to their medical care. Major complications which were life threatening or a contributory cause of death occurred in 5 per cent of these patients. Schimmel's rather high and worrisome figure of 20 per cent complications also included adverse reactions to digitalis and insulin, both of whose actions have long been familiar to the profession. Olin[6] recounts a review of the growing problem of iatrogeny defining not all but some of the more unusual and interesting ones in the field of neuropsychiatry metabolism, genetics, gastrointestinal tract, hematology, surgery and cancer.

In the field of neuropsychiatry behavioral disorders abound following the use of drugs.[6] Grandiose delusions and hyperexcitability can result from ACTH injections or steroids. Impulse rage reactions can occure from amphetamines used in obesity. Acute psychosis with agitation can result from meprobamate withdrawal. Psychotic depression and suicidal tendencies can be induced by reserpine. Drug induced neurologic disorders can also affect muscles.[7] Overdosage as well as drug withdrawal has been noted with meprobamate, cycloserine, chlorprothaxine (taractan) and specifically convulsive disorders following certain phenothiazines.

Tranylcypromine (parnate) and pargyline HCl. (Eutonyl)—Monoamine oxidase inhibitors may precipitate "paradoxical" sudden severe hypertension with intracranial bleeding when used with amphetamines, other monoamine oxidase inhibitors or foods high in tyramine such as aged cheese. True papilledema with increased intracranial pressure may be induced by steroid therapy. This therapy has been described as a cause of pseudomotor cerebri in children and it is occasionally seen in adults leading to unnecessary extensive investigations.

Isoniazid can induce peripheral neuropathies unless pyridoxine is used. Nitrofurantoin can result in peripheral neuropathies in patients with chronic renal failure. Brachial plexus paralysis has been reported following the use of tetanus antitoxin, whether there is or is not accompanying serum sickness. Finally myopathies can be caused by triamcinolone therapy and they seem to be related to the fluorine atom in the alpha 9 position since they have also been observed after the use of dexamethasone.

Metabolic iatrogeny can be induced by medications and their cause go unrecognized. Thiazide diuretics can induce hyperuricemia with gout and hyperglycemia in diabetics and even nondiabetics. Oral hypoglycemic agents such as chlorpropamide can cause prolonged and severe hypoglycemia which may be confused with stroke especially in elderly patients. Gynecomastia may result from therapy with digitalis, or spironolactone. Outdated tetracyclines can cause an adult-type reversible

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Contraindications: Porphyria, peptic ulcer, ulcerative colitis, mental depression, sensitivity to either component. *Precautions:* Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression. Observe for signs or symptoms of peptic ulcer or ulcerative colitis. Discontinue at first sign of mental depression; keep in mind possibility of suicide. Exercise extreme caution in history of mental depression. May produce cardiac arrhythmias when used with digitalis and quinidine, or may precipitate biliary colic in patients with gallstones. Discontinue 1 to 2 weeks before surgery; inform the anesthesiologist in event of emergency surgery. Exercise caution in history of epilepsy. Discontinue 1 to 2 weeks before ECT.

Adverse Reactions: Drowsiness, skin rash, "hangover," systemic disturbances, increased salivation and gastric secretion, nausea, vomiting, increased intestinal motility, loose stools, angina-like syndrome, arrhythmias, bradycardia, flushing, hypotension, nervousness, paradoxical anxiety, rarely atypical Parkinsonian syndrome, central nervous system sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis and optic atrophy), dryness of mouth, syncope or dizziness, epistaxis, purpura secondary to thrombocytopenia, asthma in susceptible persons, nasal congestion, weight gain, and impotence or decreased libido.

Usual Adult Dosage: Initially, 1 to 4 tablets daily for one week; maintenance, 1 to 2 tablets daily.

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Fanconi's syndrome with proteinuria, glycosuria and amino-aciduria.

Busulfan used in long-term treatment of chronic myelogenous leukemia or macroglobulinemia of Waldenström can cause clinical Addison's disease but with normal steroid blood levels. Cushing's syndrome with all its sequelae has been produced from use of high doses and prolonged use of steroids. Last but not least is hypercalcemia with a confusing clinical picture of lethargy weakness, renal insufficiency and coma which can result from Vit D intoxication, from milk-alkali, from estrogen therapy for cancer of the breast or prostate with skeletal metastases.

L.H.N.

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This Blight Of Noise

During the last thirty years much attention has been given to the effects of various sound intensities upon the hearing acuity of workers and maximum permissible levels of sound intensity for factories and offices have been established by regulation. But in relation to the home environment until very recently there has been no evidence that design and operational criteria for any single unit in the home need be examined other than for performance and salability. No attention whatever was given to its operational sound intensity. Nevertheless the necessity and desirability of control of sound in the home was emphasized as long ago as 1938 by McCord who spoke of the multiple and insidious ill effects of noise and its inadequate recognition. Noise, he said, constitutes a baneful influence on lives of millions of persons throughout the country especially those who live in urban centers.

Noise deafness constitutes the most serious and tangible of the ill noise effects (echoserosis). There is in addition, however, a host of scarcely measurable injuries made evident by neurosis, loss of sleep, excessive fatigue, emotional disturbances, that jeopardizes the complete well-being of most persons and in which noise does play a part. Farr[1] has called attention to the mechanical devices in the home as sources of noise which could be of significance in health impairment. He has called attention to the annoyance value of sound-unexpectedness, interference, inappropriateness, intermittences, reverberation and also its origin. Self-generated sounds are well tolerated by the individual generating it, but sound generated by another person or an impersonal sound such as sonic boom has a very high annoyance value. It seems to amplify each of the above qualities responsible for annoyance.

Age is another factor leading to sound becoming annoying and irritating, for at advanced age most people have a loss in hearing acuity. This makes it likely for extraneous sounds to cause interference in communication even when the extraneous sound is of low intensity. This inability to discriminate effectively between some sounds even of equal intensity may lead to social embarrassment and this in turn can lead to changes in patterns of behavior in efforts to mitigate the degree of interference. The behavioral changes are assumed in order to temper the source of embarrassment to the person who suffers from loss of hearing acuity.

The teenager with hearing acuity can listen to loud television, hear a telephone in the distance in the midst of a varied mixture of high intensity enviromental sound. He can select at will the desired sound from a complex of heterogenous sounds in the background and reject the undesired sound. The person with loss of hearing acuity is unable to clearly distinguish when background noise is high, as at a social gathering. He can't readily discriminate and select out of conversational sound from an adjacent person speaking. It will require a major effort in an older person. This inability to distinguish what is said can well result in rejection of participation in such gatherings. High and complex noise levels in the background may be traumatic because it transcends his speech interference level. Sounds of such intensity are made by many household devices in present-day living quarters and are capable of generating sounds quite in excess of that necessary to transcend the speech interference level and of interfering with other types of sound communication as well.

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Contraindications: Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease or impending hepatic coma (hepatic coma due to hypokalemia has been reported in patients on thiazides). Do not use Enduronyl in severe mental depression, suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity where there is history of allergy or asthma. If added potassium is indicated, dietary supplementation is recommended. Reserve enteric-coated potassium tablets for cautious use only when necessary, as they may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation often requiring surgery; discontinue them immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occurs. Neither Enduron nor Enduronyl contains added potassium.

Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

EUTRON™ Each tablet contains Pargyline Hydrochloride 25 mg. with Methyclothiazide 5 mg.

Indications—Moderate to severe hypertension.

Contraindications—Pheochromocytoma, paranoid schizophrenia, hyperthyroidism and advanced renal failure. Not recommended in malignant hypertension, children under 12, pregnant patients.

Do not use with: centrally or peripherally acting sympathomimetic drugs; foods high in tyramine (e.g., aged and natural cheeses); parenteral reserpine or guanethidine; imipramine, amitriptyline, desipramine, nortriptyline or their analogues; other monoamine oxidase inhibitors; methyldopa or dopamine; separate Eutron and these agents by two weeks.

Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease; impending hepatic coma from thiazide-induced hypokalemia.

Warnings—Patients: 1. No other drugs (particularly "cold preparations" and antihistamines), cheese or alcohol without physician's consent. 2. Promptly report orthostatic symptoms, severe headache, other unusual symptoms. 3. Angina pectoris or coronary artery disease patients must not increase physical activity with improved anginal symptoms or well-being.

Physicians: 1. Use antihistamines, hypnotics, sedatives, tranquilizers and narcotics (meperidine contraindicated) cautiously in reduced doses. 2. Stop Eutron two or more weeks before elective surgery; in emergency surgery reduce premedication (narcotics, sedatives, analgesics, etc.) to 1/4 to 1/5; carefully adjust anesthetic dosage to patient response. 3. Use cautiously in advanced renal failure. 4. Pargyline may induce hypoglycemia. 5. Consider possible sensitivity reactions when a history of allergy or asthma is present. 6. If potassium is indicated, dietary supplement is recommended; enteric-coated potassium tablets may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation frequently requiring surgery; discontinue medication immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occurs; Eutron does not contain added potassium. 7. Possible systemic lupus erythematosus has been reported for thiazides.

Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804438R

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Home designers have paid no thought to the noise problem. They have turned the kitchen into miniature transient simulators of boiler factories, the ventilating fan over the stove, the dishwasher, the garbage disposal unit, the blender, the refrigerator with three motors all make significant contributions to sound which is reflected by steel cabinets, hard plastic covered surfaces and caused to reverberate. A tired, taut person will certainly not leave such a kitchen pleasantly relaxed nor do the roars, squeaks, whirrs and wheezes issuing from it lead to quiet contemplation of pleasant meals by those who are waiting.

In many apartments sound intensity is of such loudness that conversation in the living room is virtually impossible while some of the devices are in operation. In a large living room a vacuum cleaner raised the sound level from 50-73 db when the nozzle was fully engaged in the rug, but when this was lifted the intensity rose to 81 db. The occupants of this household consider hi-fi record player to be very loud at 80 db. Neither have the bedrooms and bathrooms escaped this blight of noise. Bedroom air conditioners, bathroom ventilating fans, poorly designed plumbing all make their contribution to this melee of sound.[2] [3]

The effect of noise in exacerbating disease is deleterious, real and immediate. What does a sound do to a case of tetanus? In other disease states such as anxieties, duodenal ulcer and other kindred so called tension ills the additive deleterious effect of noise is unquestioned. Any disease which may be associated with an emotional change requires as part of the therapy a calm, relaxed, quiet environment. It is particularly true of disturbed emotional states. Psychiatrists and hospital administrators are well aware of this problem.

Loudness is not a necessary quality of noise. Sound must jar the mood to become noise and if it does so then noise results whether the sound be a classical rendition of Bach or a soft off-key hum of a contented person. Cacophony resulting from several radio and TV turned to low intensities but a variety of programs can lead to a most annoying experience for the involuntary listener and may be just as destructive of sleep as a loud shot. The trauma of noise may bring to the surface a scarcely submerged tension and result in an emotional outburst or it may provoke symptomatology.

Denzel has stated "noise interferes with rest, relaxation and especially with sleep. Sleep is complete withdrawal from the world around us and is an obvious necessity for physical and emotional health. Less complete withdrawal into quiet of our homes may also be necessary. If we want to attain individual integrity, we need to reduce the sound level of our modern environment."[4 5]

It is time that man realizes that his home can be designed to acoustic criteria resulting in a pleasant environment for him and medically conducive to a state of well-being permitting him to relax, refresh, restore and re-invigorate himself for the tasks, chores and strains of life. Clearly it is time for the physician to join up with the acoustic engineer, the architect and the decorator, to establish general acoustical standards for personal environment as has already been done for factories and offices and well run hospitals.

L.H.N.

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The Carcinoid Syndrome: Serotonin And Mental Function

Parachloralanine (PCP) is a potent and selective depletor of tissue serotonin in animals. The drug acts by inhibiting the hydroxylation of tryptophan to 5 hydroxytryptophan, (5HTP) which is the first and rate limiting reaction in serotonin biosynthesis.[1] With the introduction of this drug we can effectively inhibit the formation of serotonin and reduce the pharmacologic effects of this amine in patients with the carcinoid syndrome since increased serotonin production is a hallmark of this syndrome. As a byproduct one would expect also to learn something about the role of serotonin in the function of the central nervous system where this amine can be found in abundance.

Engelman and his colleagues[2] have just reported on the use of PCP in five patients with the carcinoid syndrome. Their studies on the five patients were models of acute clinical observation and biochemical analysis of blood and urine for content and metabolites of serotonin. They found that 3-4 grams of PCP inhibited serotonin production by 72-88 per cent, noted within one to three days. After treat-

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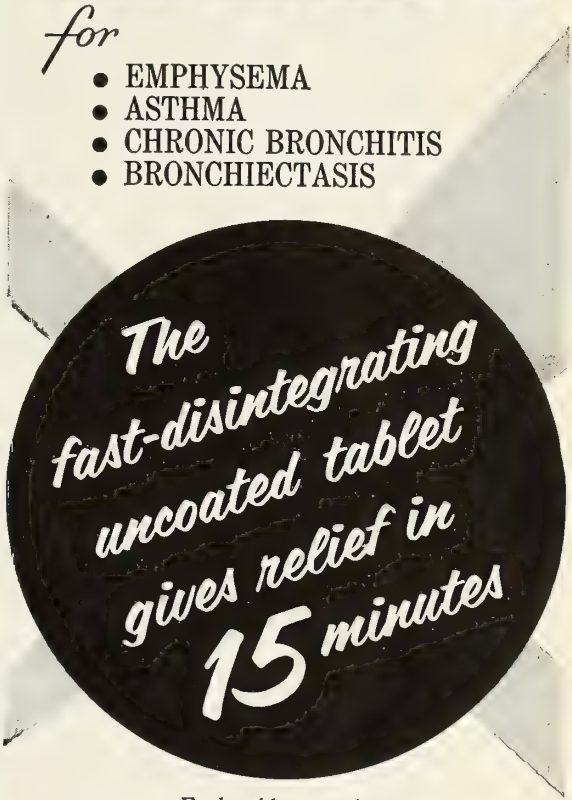

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ment was stopped the symptoms slowly returned. The drug produced an amelioration of the severe gastrointestinal disturbances over a long period without any evidence of drug toxicity. In one case it was not well tolerated because of onset of severe headache, deterioration of mental function and psychic depression. In several other cases there were also disturbances of central nervous system function.

The therapeutic effects, therefore, were good in affording relief of gastrointestinal symptoms, but poor as far as central nervous system function was concerned. These latter were also observed by Cremata and Koe[1] in subjects treated with PCP, namely tiredness, dizziness, anxiety and headache. With higher doses they noted distinct psychic effects ranging from depression to hallucination, effects which could well be related to altered serotonin metabolism. It should be noted that the patients with carcinoid did not exhibit central nervous system symptoms even though they all had high plasma serotonin levels. The probable answer is that serotonin does not readily penetrate the blood brain barrier. However, PCP does prevent serotonin synthesis and one would expect that it would deplete brain serotonin levels.

The role of serotonin in brain has been debated for many years. Originally it was speculation arising from experiences with LSD. When it was discovered that LSD antagonized certain effects of serotonin on smooth muscle, it led Woolley in this country and Gaddum in England to hypothesize that perhaps the toxic psychoses caused by LSD and even endogenous psychoses might be due to depletion of serotonin in the brain. This speculation was reinforced when it was demonstrated that reserpine and iproniazid which under certain conditions depressed or elevated mood did so by effecting the levels of serotonin, depletion with reserpine and elevation with iproniazid.

The only complicating feature was that these substances also affected the brain levels of norepinephrine and other biogenic amines and it was difficult to separate the effects of norepinephrine on mental states from that of serotonin. In consequence the evidence for the involvement of serotonin in mental function became somewhat obscure. The recent availability of more specific pharmacologic tools, alpha-methyl-tyrosine which blocks norepinephrine synthesis and PCP which blocks serotonin synthesis has made it possible to obtain profound decreases in the availability of one of the amine without affecting the other appreciably.

Studies with alpha methyl tyrosine over the past two years by depleting norepinephrine in brain have suggested that this bioamine is involved in repetitive responses in conditioned avoidance behavior and in some of the behavioral effects produced by amphetamine and possibly in arousal. On the other hand data on the effects of PCP on behavior in animals have not been too significant to support many inferences of serotonin involvement. Its effect on conditioned avoidance or on general behavior has not been striking. In the doses employed it did not produce sedation in itself and did not prevent characteristic effects of reserpine which, therefore, cannot be attributed to serotonin. The only clear behavioral effect in animals appears to be suppression of sleep which is correctable by administering a serotonin precursor, 5 hydroxytryptophan which can traverse the blood brain barrier. Jouvet[3] reported that PCP administered to cats results in striking insomnia and two of Engelman's patients also exhibited this symptom.

The report by Engelman on the use of PCP in patients with carcinoid syndrome is of considerable interest. In the first place the agent was useful in counteracting some of the unpleasant symptoms of the disease. Secondly, the observation of subjective changes associated with the large dose required may throw some light on the function of serotonin in the brain. With such doses a variety of subjective symptoms were noted including listlessness, depression, insomnia, anxiety, confusion, delusions and hallucinations. Previous reports on smaller doses did not uncover these striking mental observations.

To be sure, the number of patients is small and some had a history of previous mental symptoms. Furthermore, these may have been biochemical effects (elevated levels of phenylalanine) in addition to depletion of serotonin which may have produced symptoms also. A longer series of patients with less associated mental disturbances and a single reduction in cerebral concentrations of serotonin are needed. If they also show disturbances in mental state, we would then have strong support for the hypothesis that serotonin is important to normal psychic function and its reduction should lead to psychic disturbances. In that case the speculation of Woolley and of Gaddum regarding the mechanism of the hallucinogenic properties of LSD (antagonism of serotonin action) would receive some re-enforcement.

We would, however, be far from supporting the further assumption that disturbances in serotonin distribution or metabolism were involved in one or more of the major psychoses. Obviously a biochemical field is open for study of biochemical basis of mental function both normal and abnormal.

Engelman's study has moved us from acute clinical observation to basic science. It is a beautiful example of the unseparability of basic science and practical medicine.

L.H.N.

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Some Consequences Of Medicare

Most industrial societies starting with Germany in the late nineteenth century provide some form of compulsory health insurance. On July 30, 1965, this country joined virtually all other industrialized countries by enacting Medicare under Social Security for people 65 years of age and older. The law's supporters looked on it as the only sensible way to provide adequate medical care for the elderly. Its opponents saw it as an unwarranted first step towards governmental control of doctors. The law has now been in effect for almost two years and it seems proper to consider some of its consequences.

Doctors are paid on the basis of reasonable (usual and customary) fees. However, institutions are paid on the basis of allowable costs plus an allowance of a fixed percentage. The choice of physician is not restricted but institutions must meet standards equivalent to those of the Joint Commission on Accreditation and must practice utilization review.

Title XVIV of the Medicare law provides funds to help the states pay all medical expenses of the "medically indigent" of all ages. For a state to be eligible for funds it must have started such a program by no later than July 1, 1967 and must at least include all those receiving assistance under other programs, that is, disabled, aged, blind and needy children. By July, 1975, the program must cover all the medically needy and must provide them with comprehensive medical care. The federal share is drawn from general revenues and contributes half of administrative costs, three quarters for training and salaries of medically skilled administrative personnel and half to five-sixth of medical costs depending on the states per capital income. Payments of doctors may be based on usual and customary fees, or on a fee schedule.

This portion of the law Title XVIV was supported by the AMA representative in Senate Committee hearings in the spring of 1965 and some of their suggestions were incorporated into it. When fully implemented, it will most probably be costlier, more controversial and of greater social significance than Title XVIII. It may also prevent further extension of the compulsory insurance portion of Medicare. It is, however, too soon to measure its effect with accuracy.

Since the Medicare law went into effect a number of consequences of it became clear as regards medical care of the elderly. Older patients are receiving better attention and are getting it more often. They do not need to hesitate to seek medical attention because of cost. If they are indigent, they now realize they are not imposing on the doctor when he treats them and they have confidence that they are receiving full and proper medical attention, not short-changed. If they need to go to a hospital, they can assume that it has met strict accreditation requirements and that their stay will be subject to utilization review. The outpatient clinic must provide them with care that is worth what the Government is paying. The nursing homes they enter must be of high quality to receive them. Their diagnostic tests can be done only in an approved laboratory.

There are some unfortunate consequences. The shortage of doctors has become more acute. Doctors are seeing more patients over 65 and more often. Besides being busy with patient care the doctor has had to assume a large burden of paper work and committee activity that the law requires. Hospitals have also acquired new problems. Besides some overcrowding the voluntary hospitals are unhappy since the 2 per cent allowance over costs that they are paid by Medicare does not provide adequately for development. Proprietary hospitals are better off because they are given an additional allowance based on a 7.5 per cent return on investment.

It is not necessarily true that the resistance of doctors generally to the passage of the Medicare law delayed its passage. However, it is probably true that without the resistance of organized medicine a less sensible program might have been initiated sooner. The great fear of doctors that they would lose professional or economic freedom as a result of compulsory insurance has not yet materialized. We have sustained a loss of the opportunity to give, that is to take care of certain patients at a reduced fee or no fee and, therefore, to feel ennobled. We are being financially compensated for this loss, but many will think it is probably a poor trade.

Most doctors seem to have adjusted themselves to the necessity of living with Medicare. There are some who wonder why they ever resisted it in view of their increased income. Most doctors also remain convinced that it is the beginning of complete governmental control of medicine and one further step in the disintegration in the values of society. Doctors are, however, cooperating with the requirements of Medicare and are now willing to take personal responsibility for its successful administration.

For the future most doctors would undoubtedly prefer that there be no extension of Medicare to those under 65 and would also prefer that the pattern of paying usual and customary fees not be altered but should serve as a basis for any future arrangements between the medical profession and insurance vendors. The possibility of extension of Medicare to include the population under 65 we realize is less subject to the influence of any acts by our profession and will probably depend mainly on the state of the national economy and on popular demand, the forces that brought Medicare itself into law.

If, however, it did come to pass and if it did include doctors' fees, the chances are that it could threaten the customary fee policy for there would then be no large group of private payers to serve as a restraint upon the raising of fees or as a criterion to define customary fees.

New problems are bound to arise in medical economics. The AMA and state societies will need to be strong and also flexible so that we can respond properly for future needs. We will probably need disinterested advice of lawyers and social scientists to supplement our own unavoidable self-interested judgments.

Many concerns lie ahead. Our profession renders a service that by virtue of its excellence in curing sickness and prolonging the quality of life is increasingly regarded as a basic human right. The manner of payment is but a part of the larger problem of supply of services. There is the need of training and distribution of doctors, nurses, social workers and paramedical personnel, the local and regional planning and operation of hospital programs, the creation of facilities for diagnosis and treatment for such diseases as cancer, heart disease, mental illness, the expansion of public health services, nursing services, convalescent services and programs for research.

All are being challenged by the rapid increase in the number of people to be cared for and in the growing complexity and cost of the care that must be given. These matters are of great concern, have been brought to the fore by Medicare and will surely be of great concern to our profession as we are being called to help in their solution. It will be up to us who are the only ones who can deliver the medical care needs, to see to it that federal control over our work doesn't happen.

L.H.N.

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Ectopic Hormone Production

It is of immediate interest to the clinician as well as of theoretical interest that malignant tumors not arising from endocrine tissue are capable of synthesizing hormones which give rise to syndromes of endocrine hyperfunction. A wide variety of tumors may produce hormones and most important in this respect are the undifferentiated oat-cell lung carcinomas. It is interesting that the most frequently formed hormones are the polypeptides. Some are ACTH, ADH, TSH ordinarily of pituitary origin. But chorionic gonadotrophin, parathormone, erythropoietin, insulin and others may also be of ectopic origin.

After Liddell demonstrated that oat-cell bronchial carcinoma produce a substance similar to ACTH which leads to Cushing's syndrome, other workers subsequently identified ACTH in various other types of tumors accompanied by Cushing's syndrome. Further studies revealed an increase ACTH level in the serum and ectopic Cushing's syndrome is invariably found associated with hypertrophy of the adrenal cortex, higher blood cortisone levels and increased urinary excretion of 17-hydroxycortico steriods. As would be expected the anterior lobe of the pituitary body contains little or no ACTH for the physiologic feed-back mechanism does not function. The ACTH is of ectopic origin.[1]

Chorionic gonadotropin is normally found in the plasma and urine of pregnant women since it is produced in the placenta. High gonadotropin levels may also be found in the presence of benign and malignant tumors of the placenta and chorionic carcinomas, teratomas of the testis or hypophysis. Ectopic sources of gonadotropin have also been described in malignant liver tumors, adrenocortical tumors, breast cancer, and malignant melanoma. Bronchial carcinoma is a common source of gonadotropin. Fusco,[2] et al detected increased secretion of gonadotropin in bronchial carcinoma and Faiman,[4] et al actually demonstrated by a radio immuno assay method an arterio venous difference in hormone concentration across a bronchial tumor bed. It thus seems clear that tumors without trophoblastic elements may also be ectopic sources of gonadotropin. Not only gonadotropin but TSH has also been shown in the extract of a metastasing bronchial carcinoma in a single observation by Hennen.

It is relevant to bear in mind that conditions of hormonal hyperfunction are observed in the presence not only of malignant, but sometimes also of benign tumors. Perhaps the most striking example of ectopic hormone production is one of the most common of endocrine disorders, hyperthyroidism. The plasma of patients with exophthalmic goitre is known to contain a substance designated as long acting thyroid stimulator (LATS) that does not originate in the anterior pituitary but most probably in the lymphocyte.[3] This substance is a gamma globulin and is thus not identical with TSH produced in the anterior pituitary gland. Nevertheless, its effect on the thyroid differs only in few respects from that of TSH proper. LATS may, therefore, be regarded as a hormone that is produced in a tissue (the lymphocyte) that under normal conditions does not synthesize LATS or TSH. LATS, however, produces hyperplasia of the thyroid and hyperthyroidism. The excess thyroid, hormones liberated now suppress normal TSH production and the pituitary now plays no role in the hyperthyroidism.

An attempt to explain the phenomenon of ectopic hormone production can be no more than a hypothesis. One plausible interpretation is that each cell contains the same DNA information and is originally capable of synthesizing an unlimited number of specific proteins, one of which is a given hormone. One of the effects of differentiation is then that a given type of cell is restricted in its function to the production of only a limited number of proteins. Certain of the regulator genes which cause the structural gene via the operator genes to release messenger RNA are repressed. It

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It is not always true, however, that an ectopic hormone is synthesized by a tissue normally incapable of doing so. In certain cases neoplastic tissue may be histologically similar to that of the endocrine organ. Thus Fusco, et al have given a description of lung carcinoma that synthesized chorionic gonadotropin and serial sections of which were found to contain areas closely resembling a chorionic carcinoma.

It is clear that when symptoms of excessive hormone production occur in any patient, the excessive hormone production may under certain circumstances justify a systematic research for a malignant tumor.

L.H.N.

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Infectious Diseases As Weapons

When a war is unjustified it is pointless to labor the relative immoralities of napalm, nuclear war or biological warfare. Even on the premise of a just war, napalm with its destructive effect on civilians is terrible enough but all-out nuclear war or biological warfare is unthinkable. Some scheme of international disarmament with inspection safeguards is now being pursued tirelessly for the nuclear weapons. However, given the nature of biological warfare and the publicity it has received there should be more awareness by the medical profession of the consequences of massive use of biological weapons. For it is we who will be called upon to treat the victims assuming, of course, that we ourselves will escape.

The history of most wars is replete with "natural examples of biological warfare." The constantly rising malaria toll in Vietnam takes more American troops out of action than does enemy fire. In both World War II and the Korean war infectious diseases were more effective than battle injuries in knocking troops out of combat.[1] Thus it is clear that even the minimum controlled application of infectious diseases as weapons would be decidedly superior to conventional warfare, and the potentialities theoretically are more grisly even than nuclear war.

The atomic bomb dropped on Nagasaki weighed five tons and killed 80,000 people but only a fraction of an ounce of chick embryo tissue inoculated with Coxielli burnetti the microorganism causing Q fever could infect a billion humans and kill as many as 10 million. Ten pounds of the concentrated food poisoning agent botulinum toxin as harmless looking as two five pound bags of sugar, could be tossed into a reservoir and despite the dilutions of millions of gallons, kill up to 65 per cent of those drinking as little as one cup of water from that source.

Why then aren't biological weapons used? One obvious reason is that they are popularly considered to be agents even more terrible than napalm or nuclear bombs. But there is another perhaps more restraining reason and less moral and that is that some critical problems involved in measured delivery of infectious diseases have not yet been solved. Answers to this are being actively pursued in many biological warfare laboratories in this country and across the world. How can the enormous destructive potential that can be generated in an ounce of embryo tissue be delivered to the intended victims? How can the results be predicted? Another question receiving much less attention is how to sequestrate the intended victims from one's own allies.

Some biological warfare experts are looking into a delivery system of infectious aerosols: a suspension of fine, solid or liquid particles generated from dilute suspensions subjected to great force as they are blown out of containers from a fine nozzle. This method would achieve concentrations of infection 10,000 times greater than is encountered in nature. The U.S. Army Chemical Group is taking an intense interest in a new field of research—Aerobiology. This embraces a study of large populations of microbes in airborne particles and includes technology of generating microbial aerosols and the science of the variables affecting the diffusion of microbial clouds.

The list of organisms likely to be used in aerosol weapons is large, but the preferred agents will be those that current medical practice finds difficult to

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combat such as anthrax causing almost 100 per cent fatal lung infections, a virus called Russian Spring-Summer Complex up to 40 per cent fatal and the rickettsial diseases, Q fever and Rocky Mountain spotted fever which is up to 80 per cent fatal. Inhalation of only a few such particles leads to crippling fever, petechiae and fatal penumonia and encephalitis.

The abrupt exposure of all life in a large area to infectious aerosols would be an unprecedented phenomenon in the history of epidemiology. It would be followed by an explosive wave of disease surpassing even the natural gradual build-up of virulence by infectious agents in the great historical plagues that swept away populations of Europe and Asia. Added to this forbidding picture is the fact that the loosing of an anthrax aerosol would produce virtually no familiar symptoms for about twenty-four hours at which time mortality approaches 100 per cent treated or untreated.

In addition to human populations every other living thing, plants, animals and other microbes might be exposed to an infectious agent for the first time in evolutionary history. What would the consequences of this be? Would new foci of disease be established? Would it create genetic changes in already virulent organisms increasing their toxicity? Nobody knows. The possibility pointed out by Stanford's Nobelist, J. Lederberg, is that the large scale deployment of viruses might pose a threat to the entire species of man because uncontrollable mutant forms of virus might develop.

Studies are under way by the U.S. Army as to how to disperse the aerosol, the preferred conditions for a large scale biological attack. They have employed actual field tests made with fluorescent particles and bacterial spores already. Also, studies are under way to increase the virulence of microorganisms so that the normal immune defenses and antibiotic protection will be more easily overcome, for example the typhoid-like rabbit fever organism can be bred to be streptomycin resistant and to breed some infectious organisms that can pierce the normal immunologic barrier. Now that the potentialities of microbial genetics are so vast, it is possible to alter specific genetic features by direct manipulation of the organisms genes.

Another method of spreading infection is by insect, bubonic plaque by fleas, epidemic typhus by lice, Q fever, Russian Spring-Summer Complex and Rocky Mountain spotted fever by wood and cattle ticks. Historically insect transmitted diseases have been notoriously effective in determining the outcome of military conflicts, some say even more effective than the decisions of military commanders, epidemic typhus and malaria being among the most telling.

Because of the serious threat to the human race of the use of infectious agents as weapons, The Pugwash Study Group on Biological Warfare has been clamoring to create an awareness in political and scientific circles of the grave consequences of the massive use of biological weapons.

L.H.N.

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Coxsackie B Virus Myocarditis

The Coxsackie viruses are a group of enteroviruses worldwide in distribution which appear to be frequently associated with epidemics of polio. They were named after the town in New York where the first virus group was identified and were discovered as research work was done on polio. They were divided into two groups, A and B and within each group is a number of types. At least 30 are known. Group B is the more common in man. A wide variety of conditions are attributed to these viruses including aseptic meningitis, epidemic pleurodynia, herpangina, vesicular pharyngitis, encephalitis, hepatitis, an influenza-like fever and myocarditis in infants.[1]

Burch's[2] recent investigation of human autopsied hearts by immunofluorescent antibody technique indicates that myocardial involvement by the Coxsackie virus is far more common than suggested by clinical observation. This finding should make us more aware of "hidden" or dormant Coxsackie B in the mycardium, pericardium, and valves of young people. The other question raised by Burch's study is whether there is a causal relationship of interstitial myocarditis with the Coxsackie virus. With the immunofluorescent antibody technique he found 29 of 50 infant hearts had interstitial myocarditis with varying degrees of damage. Seventeen had interstitial reactions, an increase in cellularity and patchy edema. In 12 of these hearts, Coxsackie B antigens were found and each positive heart had essentially the same features of interstitial myocarditis.

None of the 12 cases of viral infection had any clinical evidence of Coxsackie B infection. Thus it is possible that this virus like the polio virus may produce a rather mild or rather chronic form of infection in which the clinical symptoms and signs are undetectable. The final prognosis in such cases is unknown. We know that the damaged myocardium in neonatal cases is repaired by fibrosis. Further study is required to determine what effect the fibrosis lesions have on heart disease later in life. Perhaps it might make up a type of the so-called idiopathic cardiomyopathy.

The cause of stillbirth and sudden unexpected death in infancy has been the subject of some investigation and much speculation.[4] Many investigators have considered a viral infection as an offending agent. Viral infection during pregnancy have been shown to be a cause of congenital malformations, low birth weight, premature interruption of pregnancy and stillbirth.[5] [6] Scattered observations in animals and man indicate that certain viral infections in pregnant women may be transmitted to the fetus, but the strain of virus is important in determining the incidence of infection.[2]

The group B Coxsackie virus is known to be infective to the intra-uterine fetus. It is highly likely that the Coxsackie myocarditis found in the three stillborn fetuses and the two infants who died within three hours after birth was caused by intra-uterine infection with Coxsackie virus B.[3] What we need is more studies of the mothers for the infection. Little has been known of myocardial involvement by the Coxsackie B virus as a source of sudden unexpected death.[4] Two of Burch's patients who died suddenly and unexpectedly had considerable myocardial damage with B$_2$, and B$_2$ B$_5$ Coxsackie virus antigen in the myocardium. Prior to Burch's demonstration of myocardial involvement such cases were diagnosed clinically as "bilateral pneumonitis", and "meningitis."

Two major clinical features of six of seven infants were meningitis and pneumonia but their hearts also showed Coxsackie B antigen. Cardiomegaly was present in one patient who had recurrent lobar pneumonia and who had Coxsackie B$_2$ and B$_5$ antigens in the myocardium. The clinical manifestations of either meningitis or pneumonia could have been related to the Coxsackie virus B. A superimposed bacterial infection in such cases often interferes with etiologic diagnostic procedures and approaches which, however, are in poor supply in general hospitals as regards viral infections.

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and, in fact, Burch also found the same pattern of incidence of the different types of Coxsackie B group antigens in the myocardium of the twelve infants and children reported here. Specific fluorescence to more than one type of Coxsackie B antigen was present in four of the twelve positive cases.

The majority of instances of interstitial or "aseptic" myocarditis reported in the literature since the original observation of Fiedler and Zuppinger (quoted by Babb, et al)[3] occurred in patients within the range of three months to three years. Saphia and Cohen reviewed 90 cases of interstitial myocarditis but in most, virus confirmation was incomplete. It seemed to them that Coxsackie B was the most likely agent since it is highly cardio-tropic and present in infancy and childhood. The diagnostic term of myocarditis described in the literature as occurring without evidence of a recognized etiologic factor and labeled variously as Fiedlers, idiopathic, interstitial, isolated or "aseptic" myocarditis as well as some case of chronic rheumatic heart disease may, in fact, be of viral origin.

It is well known that the fetus and infant of both animals and man are more susceptible to Coxsackie B than older animals of the same species. There are many well documented reports of epidemic outbreaks of Coxsackie B infections with associated involvement in maternity houses or other epidemic areas in the past decade. Burch's study indicates that the precise incidence of viral infection in infants and children is probably much higher than indicated in the literature, since as seen above he found a considerable number of cases of clinically occult Coxsackie B myocarditis in infants and children.

L.H.N.

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The President Attempts To Reshape American Medicine

Everywhere the old order changes and happy they who can change with it.—Sir William Osler, 1895.

A report released in November by President Johnson's Advisory Commission on Health Manpower suggest a basic "reshaping" of the nations health care system to hold down costs, upgrade quality and increase availability of services. It offered more than fifty recommendations among which are included proposals for widespread quality control of medicine, periodic relicensing of doctors and permanent incentives to increase the efficiency and quality of care.

The commission seems to deplore the long delays to get a doctor's appointment, long periods spent in the "waiting room," hurried and impersonal attention, uneven distribution of medical care, shortage of beds in one hospital while beds in another lie unused. All this the commission believes attest to a growing national emergency. "A health crisis is upon us." It's hard to see how these trivia add up to a health crisis. Since the President thinks the report is required reading for government agencies, it is important for all of us to be informed of its contents.

The Commission which is made up of fifteen members of which Dwight L. Wilbur of the AMA is one was remarkably unanimous in its recommendation for changing the system. The most important and in some ways the most radical recommendations involve financial incentives and penalities to increase both the efficiency and the quality of hospital care. This found wide variations in cost among hospitals, in fact more than 100 per cent in some surveys and blamed these variations on "the almost total lack of economic incentives for efficiency or mechanisms that would force the inefficient to improve or go out of business." Wide cost variations showed up in all aspects of hospital operations from nursing to purchase of pork chops.

They pointed out some current practices that actually encourage inefficiency. Medicare, medicaid, some private insurance plans like Blue Cross reimburse hospitals on a cost or cost-plus basis for care rendered their subscribers. This means that the least efficient ones receive the largest payments while th most efficient ones get less. To reverse this situation the commission recommends that the federal government and health insurance groups experiment broadly with new payment formulae.

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It suggests several approaches all based on the principal that hospitals in a given locality should get equal pay for equal service and should reap greater financial rewards as they upgrade the quality of the care they give or increase their efficiency in delivering it. The quality would be evaluated by peer groups of medical experts. Grossly inefficient hospitals would be paid less than their costs and would presumably be forced out of business unless they improve. It is significant that already amendments to the social security law are is contemplation that would enable the federal government to experiment with new formulae.

The report is laced with incentive schemes to provide "efficient" hospitals with capital funds for expansion, to encourage medical schools to expand and improve and to give doctors the key factors in determining hospital utilization, a financial stake in hospital operation and membership on hospital boards. The incentive schemes rely heavily on another set of recommendations that is bound to be controversial—the widespread use of peer review groups to monitor and evaluate the quality care rendered by hospitals and doctors. They wish to extend the present practice of tissue committees, medicare utilization committees, medical society grievance committees and other groups to institute peer reviews routinely on virtually all hospital and medical cases.

The commission also found a serious "quality gap" between the latest advances in medical science and technology and the treatment being given patients. "Deviations from best practice appear to be significant and widespread" it said. It quotes from a survey of four hundred and thirty patients admitted to ninety-eight hospitals in New York City in 1962, which found that only 31 per cent of the general medical cases received "optimal" care. And a recent survey of medical laboratories by the P.H.S. found that 25 per cent of reported results were erronious. Moreover they found that large segments of the population receive little or no care.

The review mechanisms envisioned by the commission are to operate at the local level under the supervision of professional societies. One scheme mentioned favorably is run by California's Blue Shield which uses a computer to scan its records for significant deviation from usual practice and then forwards the records of the questionable cases to the County Medical Society for investigation.

Another key recommendation of the commission includes that state governments and professional societies should explore the periodic relicensing of doctors and other health personnel to "insure that they keep up with the latest knowledge." However, relicensing may be granted on the basis of completing a continuing education program or passing a challenge examination in the physician's specialty.

The commission wants the United States to produce enough physicians to meet its own needs instead of relying heavily on 40,000 foreign trained physicians who currently comprise 14 per cent of the active physicians in this country. The production of physicians is to be increased by substantially expanding existing medical schools and building new ones. Even so they find the doctor shortage worsening because various demands cut into the amount of time available for doctor-patient contact.

Universities are urged to supervise the formal education of all health professionals including such graduate training as internships and residencies in order to eliminate the present "unco-ordinated" system in which as many as five different groups may be involved in educating a single individual. The commission further urges that programs of health care for the disadvantaged should be given highest priority.

Health insurance organizations are to provide coverage of outpatient as well as inpatient health services so that patients and doctors will no longer be inclined to press for hospitalization when less costly outpatient services would do just as well. The highest priority is urged to be given to development of methods that will assure easy access to adequate health, possibly by giving a community health organization a single ombudsman-like individual responsibility for assuring success.

It stopped short of recommending extension of prepared group practice arrangements, but it spoke favorably of such plans particularly singling out the Kaiser Foundation Health Plan in California which delivers "high quality medical care for 20 to 30 per cent less cost than the cost of comparable care obtained outside the plan."

The significance of this report is that for the first time an influential highly visible group has taken up suggestions previously expoused by occasionally "lonely voices." P. R. Lee, Assistant Secretary for Health and Scientific affairs of the department of H.E.W. points out that "the recommendations are far more radical than anything that has been proposed by presidential commission or other formal advisory groups before."[1]

The proposals are bound to provoke opposition. Hospitals that have enjoyed an easy "cost plus" world are not apt to like it. Neither are the doctors ready to judge their "peers" or to be judged by them. Many government agencies won't like it. The proposals could easily get bogged down in years of discussion. But Chairman Miller thinks the time is short. He told a press conference that the nation had "problems to solve until the early 1960's—now it has catastrophes to prevent."

Clearly the medical profession must begin serious thinking about "where we are and whither are we going."

L.H.N.

References

1. Boffey, P. M.: Health crisis: L.B.J. panel calls for reshaping American medicine. Science, 158: 1160, 1967.

Teratogenesis And Viral Infections In Pregnancy

Thalidomide and rubella are outstanding examples of the role of teratogens in the production of human malformations, the first is a drug, the second a viral agent. Accordingly our suspicion of teratogenesis should be aroused whenever a pregnant woman falls ill with an infection and whenever the expectant mother is taking drugs which may be teratogenic.[1]

Viral infection may adversely affect the course of pregnancy and result in abortion, fetal death, congenital malformation or neonatal illness. The precise sequelae of maternal viral disease depends upon the severity of the maternal infection, virulence of the infecting organism and gestational age at the time of infection. A fetal death as a result of direct fetal infection may occur in a variety of viral infections of the mother.

Rubella virus and the virus of cytomegalic inclusion disease are the two agents that have been clearly established as the cause of congenital malformations. The evidence linking influenza infection with the production of congenital defects is strongly suggestive but not as yet conclusive. On the other hand we know that a number of viral agents are capable of producing specific congenital infections. These agents include Coxsackie B, polio, herpes simplex, hepatitis, small-pox, vaccinia, measles, western equine encephalitis and chicken pox viruses.[2, 3] Virus infections that are compatible with life and become manifest only after birth or in early infancy include mental retardation and phy-

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...can be rough when epidemics of nausea and vomiting strike a family. Emetrol offers prompt, safe relief. It is free from toxicity[1] or side effects[2,3] and will not mask symptoms of serious organic disorders.

1. Bradley, J. E., *et al.*: J. Pediat. *38*:41 (Jan.) 1951.
2. Bradley, J. E.: Mod. Med. *20*:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.

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WILLIAM H. RORER, INC.
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sical defects, seizures, cerebral palsy, auditory, visual and other neurosensory disorders. Whether an infant will have a congenital malformation or an actual disease caused by the infection will be determined in part by the gestational age at the time of infection and in part by the virulence of the infecting organism. In general the earlier the viral infection, the greater the risk of damage to the fetus and the more numerous will be the types of defects.

It is probable that fetal death is the most frequent result of viral infection and that relatively a virulent viral infection is compatible with survival. The congenital malformations caused by rubella virus are the result of a relatively mild destructive process occurring at a critical period of ontogenesis early in gestation. The defects due to cytomegalic virus are caused by a more severe destructive process at a less critical period of ontogenesis, later in fetal life.

In 1964, there was a nationwide epidemic of rubella following which a wide spectrum of fetal disease due to maternal virus infection was observed. In addition to the already known congenital malformations, abortion, fetal and neonatal deaths, several new clinical manifestations were identified as defects associated with rubella infection. Many infants with congenital rubella infection were found to be "virus shedders" for many months after birth and were infectious to susceptible individuals. Several clinical patterns of congenital rubella were identified; the child with a single defect, cataract or glaucoma, pulmonic stenosis, microcephaly or deafness, the premature infant who appears normal at birth but subsequently is found to have rubella meningoencephalitis and heart disease, the infant of low birth weight with jaundice, purpura, hepatosplenomegaly, cataracts, congenital heart disease, deafness, microcephaly and chronic meningoencephalitis who continues to be a virus shedder and the ostensibly normal infant who at birth is excreting virus.[2 6]

Cytomegalic inclusion disease acquired postnatally is a common, mild, usually inapparent infection. From 30-60 per cent of women of childbearing age have serologic evidence of previous infection. If a mother acquires the disease, then during the viremic phase fetal infection occurs resulting in a high proportion of damage to the central nervous system, if the infant survives.

Fetal and neonatal Coxsackie virus infection is severe and characterized by myocarditis meningoencephalitis. The disease is acquired from the mother who had an influenza like illness late in pregnancy. Intra-uterine mumps viral infection has been described as being associated with primary endocardial fibroelastosis. Neonatal herpes simplex infection is contracted from mothers with vulvovaginitis and cervicitis during passage through the birth canal. In the mother the disease is mild and localized. In the infant it is severe, systemic and frequently fatal, with adrenal, liver and lungs most frequently involved.

First trimester infection with influenza is probably associated with increased incidence of abortion, stillbirth, premature delivery and neonatal morbidity. Although evidence for its causing congenital malformations is strongly supporting this has not yet been definitely established.[2] Infectious hepatitis, like influenza may also be more severe in the pregnant woman, especially in the late stages of pregnancy at which time there is also an increase in fetal deaths.

When smallpox was not rare the mortality rate was also higher in pregnant women and abortion, stillbirth and premature delivery were frequent. Now generalized fetal vaccinia and abortion have occurred following both primary and revaccination of pregnant women for smallpox, a potent argument against this procedure during pregnancy. There are a few recorded cases of maternal infectious mononucleosis which tended to be severe and prolonged and damage to the fetus have been reported.[8] Abortion, stillbirth, premature delivery, neonatal death and congenital infection may follow maternal measles and chicken pox infection and in fact major congenital malformations have been reported following first trimester measles infection. Maternal herpes zoster infection in the first trimester is thought to be associated with increased incidence of congenital cataracts.[2 4 5]

The moral of all this is quite clear. The gestational infections produce on the one hand congenital malformations if they occur in the first trimester and pathological changes in the heart or nervous system if the fetus contracts the disease later in its development. Here clearly are both epidemiological, medical and even moral issues to be faced.

L.H.N.

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2. Green, D. M., et al: Generalized uaccinia in the human fetus. Lancet, I: 1296, 1966.

3. Blattner, R. J. and Heys, F. M.

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Letters-to-the-Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Connecticut Deals With The Drunken Driver

To The Editor:

When a man is convicted for driving under the influence of alcohol, the Department of Motor Vehicles suspends his license for what they call an indefinite period. After the drunk driver has been six months without his license, he can apply for reinstatement, but before the Department of Motor Vehicles reinstates any drunk's license they make an investigation of the person's current drinking habits .A Department agent visits policemen, landlords, lawyers and others, and if the investigator gets reason to believe that the applicant has a drinking problem, the Department refuses to return the license. We have one man who was convicted of drunk driving over 14 years ago, and who has still not gotten his license back because the Department investigations continue time after time after time to be unfavorable. I am not sure whether this is good or bad for the individual; whether it is good or bad for society, but I thought you might be interested to know a little about how the Department operates.

David E. Koskoff, Attorney

144 West Main Street
Plainville, Conn.

Dear Dr. Nahum:

I would like to place a request for used examining tables in *Connecticut Medicine.* We need three tables with stirrups for our neighborhood Family Planning Clinics situated in low income housing projects in New Haven. Light weight easily movable tables are best suited to our needs as they are used in multi purpose rooms and must be removed when clinic is not in session.

Our clinics have used the Cancer Society's Mobile Unit until now but their own programs are conflicting with our clinics. Since we have not budgeted for heavy equipment we are now in the position of having full clinics and no tables, lights or screens. Donations of any of these items will be gratefully accepted.

Sincerely,

Dorothy Brockway, M.D.

Director Family Life Education-Family Planning
46 Webster Street
New Haven, Conn., 06511

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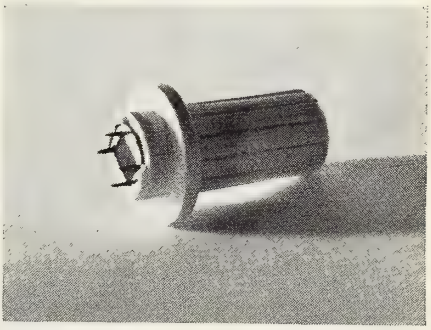

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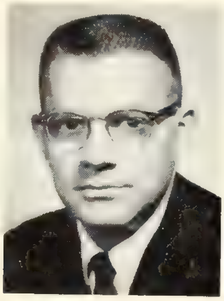
176th ANNUAL MEETING

of the

CONNECTICUT STATE MEDICAL SOCIETY

Hartford Hilton Hotel
10 Ford Street, Hartford, Connecticut
April 30, May 1, 2, 1968

COMMITTEE ON PROGRAM OF THE SCIENTIFIC ASSEMBLY



David Babbott

David Babbott, *Burlington, Vermont, (formerly Hartford) Chairman*
William F. Eckhardt, Jr., *New Canaan, Co-Chairman*
Brae F. Rafferty, *Willimantic*
Paul F. McAlenney, *New Haven*
Michael J. Esposito, *Meriden*

MESSAGE FROM THE PRESIDENT

The Connecticut State Medical Society is holding its 176th Annual Meeting on April 30, May 1 and 2. With much thought and effort, the program committee has produced an outstanding list of speakers on topics of broad interest. The business to come before the House of Delegates is more vital than ever and is of importance to every member.

An innovation this year, therefore, is the integration of the business and scientific sessions. At the Reference Committee hearings, held between the Tuesday and Wednesday scientific sessions, all members of the Society may attend and present their thoughts. It is hoped that all will avail themselves of the opportunity to participate in both phases of the Meeting. Even dancing has been added to the Annual Dinner.

Our industrious administrative staff has co-ordinated these activities and exhibits at the Hartford Hilton—for your education, for the furtherance of excellent medical care, and for your enjoyment. In these three days, we can have freer discussion and come closer together for the good of all.

E. Tremain Bradley

GENERAL INFORMATION — READ CAREFULLY

Registration

The registration desk will be located on the mezzanine floor and everyone attending the meeting is requested to register. There will be no charge for registration and all members of the Society will be given a guest luncheon ticket when and only if they register.

Parking

There are ample parking facilities at the hotel and in the surrounding area. If you wish, you may drive up to the door of the hotel and an attendant will park your car for you.

Telephone

Telephone messages will be received at Hartford 249-5611.

Luncheons

Luncheons will be served in the Cities Rooms on the Mezzanine, on May 1 and May 2 and ALL MEMBERS OF THE SOCIETY REGISTERING WILL BE THE GUESTS OF THE SOCIETY. PLEASE REMEMBER A LUNCHEON TICKET WILL BE GIVEN TO MEMBERS ONLY IF THEY REGISTER.

Hotel Accommodations

Persons who wish to remain overnight should make reservations not later than two weeks prior to opening date of the meeting. Reservations will be held until 6:00 P.M. on the day of arrival, unless later hour is specified. Please indicate in your letter that you are attending the Connecticut State Medical Society meeting. Your letter should be directed to the Front Office Manager, Hartford Hilton Hotel, 10 Ford Street, Hartford, Connecticut.

Annual Dinner and Dance

The Annual Dinner will be held at the hotel on Wednesday, May 1, 1968. The social hour will be at 7:00 P.M. and the dinner at 8:00 P.M. All persons attending the dinner will be the guests of the Society at the social hour which will begin *promptly* at 7:00 P.M. and end *promptly* at 8:00 P.M. Your reservation for dinner should be sent in as soon as possible.

Program

General scientific sessions will be held on Tuesday, Wednesday and Thursday in the Terrace Room and Section meetings will be held in the rooms listed in the program.

Exhibits

The technical exhibits will be located in the ballroom. Physicians should take advantage of the opportunity to review "under one roof" what is new and timely in the goods and services available.

ANNUAL MEETING OF THE HOUSE OF DELEGATES

Terrace Room — Mezzanine

Kenneth F. Brandon, *Hartford, Speaker of the House, presiding*
Frank K. Abbot, *Waterbury, Vice-Speaker of the House*

Tuesday, April 30

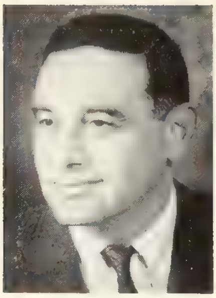
OPENING SESSION

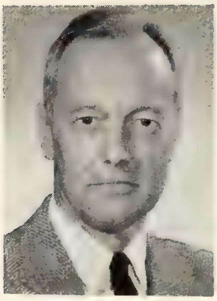
8:00 Registration
Continental Breakfast for Delegates and Official Guests
9:00 Call to Order
12:30 Luncheon for Delegates and Official Guests—Cities Rooms—Mezzanine
3:00 Reference Committee Hearings—Cities Rooms—Mezzanine
6:30 Reception and Dinner for Delegates and Official Guests
Cities Rooms—Mezzanine

Wednesday, May 1

FINAL SESSION

3:00 Registration—Terrace Room
3:30 Call to Order


Sheldon J. Segal
New York City


John M. Morris
New Haven, Conn.

SCIENTIFIC PROGRAM

Tuesday, April 30

12:30 Registration—Mezzanine
Opening of Exhibits—Ballroom—Mezzanine

Terrace Room

1:30 Call to Order—E. Tremain Bradley, *Norwalk, President of the Society*
Address of Welcome—Norman H. Gardner, *East Hampton, President-Elect of the Society*

Paul F. McAlenney, *New Haven, presiding*

1:45 Future and Present Concepts of Population Control
Sheldon J. Segal, Ph.D., *New York City; Director, Biomedical Division of Population Council, Rockefeller University*

2:45 Discussion
John McLean Morris, *New Haven, Connecticut; Professor of Gynecology, Yale University School of Medicine; Attending Gynecologist, Yale-New Haven Hospital*

3:00 *REFERENCE COMMITTEE HEARINGS, HOUSE OF DELEGATES—CITIES ROOMS*
All members of the Society invited to participate

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON INTERNAL MEDICINE

3:30 Room 420

President: James M. Grant, *Bridgeport*
Secretary: Walter S. Morgan, *New Haven*

ORGAN TRANSPLANTATION—PROBLEMS OF IMMUNOLOGY

Fred S. Kantor, *New Haven, Connecticut; Associate Professor of Medicine, Yale University School of Medicine*

Bernard Lytton, *New Haven, Connecticut; Associate Professor of Urology, Yale University School of Medicine; Chief, Section of Urology, Yale-New Haven Hospital*

Irwin H. Lepow, *Hartford, Connecticut; Professor of Pathology and Chairman of Department of Pathology, University of Connecticut School of Medicine*

Tuesday, April 30

SECTION ON PEDIATRICS
(Hezekiah Beardsley Club)

3:30 Room 416

President: Clarence W. Harwood, *Middletown*
Secretary: Estelle Siker, *Hartford*

Future Plans For The Pediatric Department—University of Connecticut School of Medicine

Martha L. Lepow, *Hartford, Connecticut; Acting Head and Assistant Professor, Department of Pediatrics, University of Connecticut School of Medicine*

SECTION ON RADIOLOGY

3:30 Room 424

President: David A. Grendon, *Sharon*
Secretary, Henry J. Fox, *Bridgeport*

Intestinal Manifestations of Systemic Disease

Arthur R. Clemett, *New Haven, Connecticut; Associate Professor of Radiology, Yale University School of Medicine*

ASSOCIATION OF MEDICAL EXAMINERS FOR CONNECTICUT

President: Samuel B. Rentsch, *Derby*
Secretary: Francis P. A. Williams, *Bridgeport*

12:00 Rooms 436-440 Luncheon For Medical Examiners, Coroners, and Guests (Dutch Treat)

1:15 Business Meeting—Election of Officers

1:45 Members Are Invited to Attend Scientific Program in Terrace Room

PROGRAM ON MEDICINE AND RELIGION—8:00 P.M. TERRACE ROOM

Arranged by CSMS Committee on Medicine and Religion

The Doctor's Dilemma in The Changing Attitudes Toward Abortion and Contraception

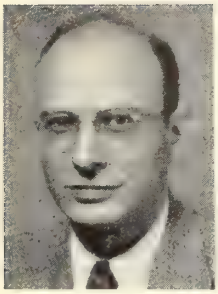
Moderator: Rev. Dr. Paul B. McCleave, ll.d., *Chicago, Illinois; Director, Department of Medicine and Religion, American Medical Association*

Panelists: Rev. Dr. Seward Hiltner, Ph.D., *Princeton, New Jersey; Professor of Theology and Personality, Princeton Theological Seminary*

John Rock, m.d., *Brookline, Massachusetts; Clinical Professor of Gynecology, Emeritus, Harvard Medical School*

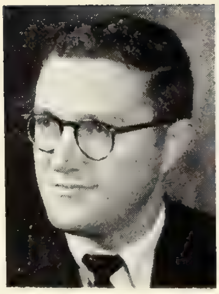
Rev. John J. Lynch, s.j., *Weston, Massachusetts; Professor of Moral and Pastoral Theology, Weston College*

Abraham N. Franzblau, m.d., Ph.D., *New York City; Psychiatrist; Dean and Professor (Emeritus) of Pastoral Psychiatry, Hebrew Union College—Jewish Institute of Religion*

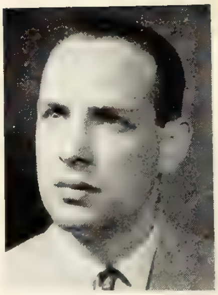


Philip K. Bondy
New Haven, Conn.

William B. Kannel
Framingham, Mass.



Robert S. Lees
New York City



Lester B. Salans
New York City

Wednesday, May 1

9:00 Registration—Mezzanine

Terrace Room

SYMPOSIUM ON ATHEROSCLEROSIS

Moderator: Philip K. Bondy, *New Haven, C.N.H. Long Professor of Medicine, Chairman, Department of Internal Medicine, Yale University School of Medicine*

9:30 A Further Report From The Framingham Study

William B. Kannel, *Framingham, Massachusetts; Medical Director, National Institute of Health, Heart Disease Epidemiology Study; Consultant in Medicine, Framingham Union Hospital*

10:15 Biochemical and Clinical Aspects of The Hyperlipidemias Associated With Accelerated Atherogenesis

Robert S. Lees, *New York City; Assistant Professor, Rockefeller University; Associate Physician, Rockefeller University Hospital*

11:00 Intermission to Visit Technical Exhibits

11:30 New Concepts in The Evaluation of Human Obesity and Its Relationship to Disordered Carbohydrate and Lipid Metabolism

Lester B. Salans, *New York City; Assistant Professor, Rockefeller University; Associate Physician, Rockefeller University Hospital*

12:15 Panel Discussion

Moderator: Philip K. Bondy
Panelists: William B. Kannel, Robert S. Lees, Lester B. Salans

1:00 Luncheon—Cities Rooms
Intermission to Visit Technical Exhibits

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON DERMATOLOGY

2:00 Room 424

President: Cleveland R. Denton, *Hartford*
Secretary: Haskell M. Rosenbaum, *Waterbury*

The Clinical Significance of Necrosis of The Skin

Samuel L. Moschella, *Boston, Massachusetts; Dermatology Section, Lahey Clinic*

SECTION ON GASTROENTEROLOGY

2:00 Room 436

President: H. David Frank, *Bridgeport*
Secretary: Saul S. Milles, *New Haven*

The Management of Fluid and Electrolyte Problems in Liver Disease

Robert S. Morrison, *Boston, Massachusetts; Director, Renal and Electrolyte Section, Lemuel Shattuck Hospital*

SECTION ON OBSTETRICS AND GYNECOLOGY

2:00 Room 404

President: Stewart J. Petrie, *Derby*
Secretary: G. Lawrence Austin, Jr., *Hartford*

History Taking and Sexual Counseling in Office Practice

Lawrence Q. Crawley, *New York City; Associate Director, Margaret Sanger Research Bureau; Chief of Sterility Clinic, Lenox Hill Hospital*

SECTION ON OPTHALMOLOGY

2:00 Room 420

President: Andrew S. Wong, New Haven
Secretary: Daniel M. Taylor, *New Britain*

Clinical Pathological Aspects of Glaucoma

Robert H. Fenton, *New Haven, Connecticut; Assistant Clinical Professor of Ophthalmology, Yale University School of Medicine*

SECTION ON PHYSICAL MEDICINE AND REHABILITATION

2:00 Rooms 412-416

President: Carl V. Granger, *Hartford*
Secretary: Sanford W. Harvey, *Middletown*

Management of Cerebral Palsied Children

Harold M. Sterling, *Boston, Massachusetts; Professor of Physical Medicine and Rehabilitation; Tufts University School of Medicine; Director, Rehabilitation Institute of the New England Medical Center*

SECTION ON UROLOGY

2:00 Room 408

President: John F. Brosnan, *New London*
Secretary: Vincent J. Longo, *New London*

PROBLEMS IN URINARY DIVERSION

BERNARD LYTTON, *New Haven Connecticut; Associate Professor of Urology, Yale University School of Medicine; Chief, Section of Urology, Yale-New Haven Hospital*

CONNECTICUT DIABETES ASSOCIATION

2:00 Room 440

President: Willem F. Van Eck, *East Haven*
Secretary: James C. Hart, *Hartford*

SERUM LIPIDS AND DIETARY FACTORS IN DIABETES

WILLEM F. VAN ECK, *President*

WOMAN'S AUXILIARY TO THE CONNECTICUT STATE MEDICAL SOCIETY TWENTY-FOURTH ANNUAL MEETING*

TOWN AND COUNTY CLUB
22 Woodland Street, Hartford

President: Mrs. Anthony P. Cipriano, *Hamden*
Recording Secretary: Mrs. William R. Richards, *Hamden* (Pro Tem)
Corresponding Secretary: Mrs. Jacques H. Green, *North Haven*

1:00 PETIT LUNCHEON
2:00 BUSINESS MEETING

Guest Speaker

MRS. THOMAS ANTON, *Old Orchard Beach, Maine, Director of the Woman's Auxiliary to the American Medical Association*

Transportation between the Town and County Club and the Hartford Hilton will be provided. Auxiliary Hospitality Room will be available at the Hotel for Auxiliary members planning to attend the Dinner Dance of the Connecticut State Medical Society.

*Inaugurating Auxiliary's Twenty-Fifth Anniversary Year

3:30 *FINAL SESSION OF HOUSE OF DELEGATES—TERRACE ROOM*
All members of the society invited as observers

INTERMISSION TO VISIT TECHNICAL EXHIBITS

Special Notice

TUFTS UNIVERSITY SCHOOL OF MEDICINE

DEAN'S RECEPTION

Wednesday, May 1, 1968

5:00 – 7:00 P.M.

SUITE 436 — HARTFORD HILTON HOTEL, HARTFORD

ALL TUFTS ALUMNI WELCOME

Wednesday, May 1

ANNUAL DINNER OF THE SOCIETY

Hartford Hilton Hotel
10 Ford Street, Hartford
Social Hour 7:00 p.m. Dinner 8:00 p.m.

Opening Remarks:

Stevens J. Martin, *Hartford, Chairman of the Council*
Norman H. Gardner, *East Hampton, President, presiding*

Presentation of Guests and Delegates from State Medical Societies

Fifty Year Membership Award
Edmund Latham Douglass, *New London*

Salute to the Woman's Auxiliary to the Connecticut State Medical Society on the occasion of its twenty-fifth anniversary year

Music for dancing, during dinner and following the program, will be provided by the Landerman Orchestra

Thursday, May 2

9:00 Registration—Mezzanine

Terrace Room

9:30 Symposium on Practical Applications of Medical Genetics

Moderator: Herbert A. Lubs, *New Haven, Connecticut; Assistant Professor of Medicine and Pediatrics, Yale University School of Medicine*

Panel:

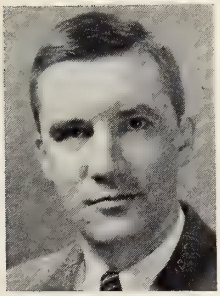
9:30 Alfred Knudson, *Stony Brook, New York; Professor of Medicine, Health Sciences Center, State University of New York*

10:15 Leon E. Rosenberg, *New Haven, Connecticut; Associate Professor of Pediatrics and Medicine, Yale University School of Medicine; Attending Physician, Yale-New Haven Hospital*

11:00 Intermission to Visit Technical Exhibits

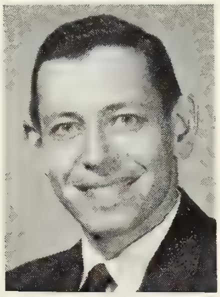
11:30 New Concepts in The Treatment of Medical Shock

Roman W. DeSanctis, *Boston, Massachusetts; Clinical Associate in Medicine, Harvard Medical* School; Assistant Physician, Massachusetts *General Hospital*

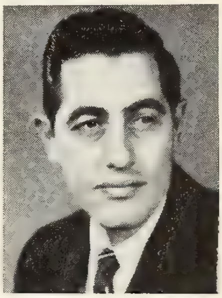


Herbert A. Lubs
New Haven, Conn.

Alfred Knudson
Stony Brook, N.Y.



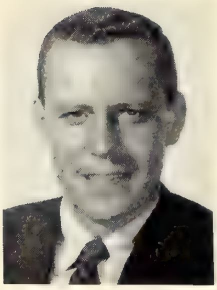
Leon E. Rosenberg
New Haven, Conn.



Roman W. DeSanctis
Boston, Mass.

Stanley M. Levenson
New York City

D. Bernard Amos
Durham, N.C.



Thomas E. Starzl
Denver, Colorado

12:15 New Concepts in The Treatment of Surgical Shock

Stanley M. Levenson, *New York City; Professor of Surgery, Albert Einstein College of Medicine; Attending Surgeon, Bronx Municipal Hospital Center*

1:00 Luncheon—Cities Rooms

Intermission to Visit Technical Exhibits

PROGRAM ARRANGED WITH THE CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

2:00-3:30 Transplantation—A Modern Perspective

Moderator: William W. L. Glenn, *New Haven, Connecticut; Professor of Surgery, Yale University School of Medicine*

Panel:

D. Bernard Amos, *Durham, North Carolina; Professor of Immunology, Duke University School of Medicine*

Thomas E. Starzl, *Denver, Colorado; Professor of Surgery, University of Colorado*

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON ALLERGY

3:30 Room 408

President: A. Arthur Fierberg, *Hartford*
Secretary: William Cohen, Waterbury

Chemical Mediators of Immediate Hypersensitivity

Martin D. Valentine, *Boston, Massachusetts; Fellow, Allergy Foundation of America, Harvard Medical School, Peter Bent Brigham Hospital*

SECTION ON ANESTHESIA

3:30 Boston-Buffalo Rooms

President: Sidney A. Chait, *Torrington*
Secretary: Harold F. Scully, *Hartford*

The Work of Ventilation

Meyer Saklad, *Providence, Rhode Island; Physician-in-Charge, Anesthesia Research Division, Department of Anesthesiology, Rhode Island Hospital*

Thursday, May 2

SECTION ON GENERAL PRACTICE

3:30 Room 424

President: Yale Gordon, *Elmwood*
Secretary: Francis Gallo, *Winsted*

BRONCHIAL ASTHMA IS COMMUNICABLE

BERNARD BERMAN, *Boston, Massachusetts; Professor, Allergy, Tufts University School of Medicine; Director Allergy Clinic, Boston City Hospital*

SECTION ON NEUROLOGY

3:30 New York Room

President: Gilbert H. Glaser, *New Haven*
Secretary: John C. Moench, *New Haven*

SYMPOSIUM—MEDICAL AND SOCIAL ASPECTS OF EPILEPSY

Speakers to be announced

SECTION ON NEUROSURGERY

3:30 Washington Room

President: Franklin Robinson, *New Haven*
Secretary: Robert H. Sturman, *Waterbury*

PERCUTANEOUS RADIOFREQUENCY CERVICAL CORDOTOMY

ROBERT H. STURMAN, *Waterbury, Connecticut; Chairman, Section of Neurosurgery, Waterbury and St. Mary's Hospitals*

JOSEPH S. SADOWSKI, *Hartford, Connecticut; Assistant in Neurosurgery, St. Francis Hospital*

SECTION OF ORTHOPEDICS

4:00

Hunt Memorial Building

230 Scarborough Street, Hartford

President: James M. Cary, *Waterbury*
Secretary: Charles T. Flynn, Jr., *Meriden*

SYNOVECTOMY IN RHEUMATOID ARTHRITIS-INDICATIONS, TECHNIQUE AND RESULTS

THEODORE POTTER, *Boston, Massachusetts; Chief of Orthopedics, Robert Breck Brigham Hospital; Associate Professor, Orthopedic Surgery, Boston University School of Medicine*

SECTION ON OTOLARYNGOLOGY

3:30 Room 416

President: Charles A. Tucker, *Hartford*
Secretary: Robert S. Rosnagle, *New Haven*

RECENT ADVANCES IN LARYNGOLOGY

GEZA J. JAKO, *Boston, Massachusetts, Assistant Otolaryngologist, Massachusetts Eye and Ear Infirmary*

Thursday, May 2

SECTION ON PATHOLOGY

3:30 Room 412

President: John L. Meyer, II, *Putnam*
Secretary: Roger K. Gilbert, *Waterbury*

PATHOLOGY OF THE PLACENTA

SHIRLEY G. DRISCOLL, *Boston, Massachusetts; Pathologist, Boston Hospital for Women (Lying-in Division), Assistant Clinical Professor, Department of Pathology, Harvard Medical School*

SECTION ON PROCTOLOGY

3:30 Room 404

President: Bernard J. Kaplan, *Hartford*
Secretary: Sanford Savin, *Bridgeport*

HIGH INTERMUSCULAR RECTAL ABSCESS

JACK W. McELWAIN, *Bethpage, New York*

CONNECTICUT DISTRICT BRANCH–AMERICAN PSYCHIATRIC ASSOCIATION

3:30 Rooms 436-440

President: John H. Houck, *Hartford*
Secretary: Robert S. McKnight, *Hartford*

The program will be a panel discussion keynoted by several well-known speakers in the areas of psychiatry, obstetrics, and law regarding the issues of sterilization and therapeutic abortion trends. The impact of these procedures and affects on the woman will also be reviewed.

CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

President: George A. Fowler, *Sharon*
Secretary: William A. Whalen, *Willimantic*

2:00-3:30 Terrace Room—(See General Program—Thursday, 2:00 P.M.)

3:45 INTERMISSION TO VISIT TECHNICAL EXHIBITS

5:00 SOCIAL HOUR—Terrace Room

6:00 DINNER—Terrace Room

Guest Speaker:

GUY OWENS, *Head, Department of Surgery, University of Connecticut School of Medicine*

TECHNICAL EXHIBITS

Space	*Firm*	*Location*
1	Ortho Pharmaceutical Corp.	Raritan, N.J.
2	Ayerst Laboratories	New York, N.Y.
3	Merck Sharp & Dohme	West Point, Pa.
4	E. R. Squibb & Sons	New York, N.Y.
5	Arthur W. Eade Insurance Agency	Hamden, Conn.
6	Surgeons' & Physicians' Supply Co.	Boston, Mass.
7	Eli Lilly and Company	Indianapolis, Ind.
8	Brookes Research Associates	Hanover, N.J.
9	Ciba Pharmaceutical Company	Summit, N.J.
10	The Silver Hill Foundation	New Canaan, Conn.
11	Mead Johnson Laboratories	Evansville, Ind.
12	Professional Equipment	New Haven, Conn.
13	Abbott Laboratories	North Chicago, Ill.
14	Ferranti-Dege, Inc.	Cambridge, Mass.
15	Mutual of Omaha	Hamden, Conn.
16	Hoechst Pharmaceutical Company	Cincinnati, Ohio
17	Parke-Davis & Company	Detroit, Mich.
18	Committee on Medicine and Religion	
19	Bristol Laboratories, Inc.	Syracuse, N.Y.
20-21	Connecticut Dairy, Food Council	Hartford, Conn.
22	Sandoz Pharmaceuticals	Hanover, N.J.
23	Smith Kline & French Laboratories	Philadelphia, Pa.
24	Encyclopaedia Britannica, Inc.	Chicago, Ill.
25	The D. G. Stoughton Company	West Hartford, Conn.
26-28	Connecticut Physicians' Art Association	
29	Center Laboratories, Inc.	Port Washington, N.Y.
30	William H. Rorer, Inc.	Fort Washington, Pa.
31-33	Connecticut Physicians' Art Association	
34	Connecticut Medical Political Action Committee (COMPAC)	
35	The Upjohn Company	Kalamazoo, Mich.
36	G. D. Searle & Co.	Chicago, Ill.
37-40	Connecticut Physicians' Art Association	
41	The Coca-Cola Company	Atlanta, Ga.
42	Syntex Laboratories, Inc.	Palo Alto, Calif.
43	Lessere-Wertheim, Inc.	Hartford, Conn.
44	Warner-Chilcott Laboratories	Morris Plains, N.J.
45	Group Insurers, Inc.	New Haven, Conn.
46	Dictaphone Corporation	Rye, New York
47	Medi/Card, Inc.	Stamford, Conn.
48	Barrington Research Associates	Princeton, N.J.
49	3M Business Products Sales, Inc.	West Hartford, Conn.

Artists — Attention !

GENERAL INFORMATION: The Connecticut Physicians Art Association is planning the 1968 Art Exhibit in conjunction with the annual meeting of the Connecticut State Medical Society. At a recent meeting of this association, the following information is submitted for guidance to art hobbyists.

WHERE: Hartford Hilton Hotel, Hartford, Conn.

WHEN: April 30, May 1, 2, 1968.

ELIGIBILITY: Physicians (members of Connecticut State Medical Society) and their families are cordially invited to join this group of art hobbyists. (In the case of children and other members of physician's family, kindly indicate relationship to sponsor). All previous exhibitors are invited to show their works at this meeting and new exhibitors are cordially welcomed. Works eligible will include oil, water color, tempora, black and white and etchings, photography, pastels, collages, mixed media and sculpture. Paintings over 24 x 30 will be hung only at the discretion of the art committee depending upon available space.

JUDGING: Art works will be judged in four categories; 1. children under 16 yrs. (children over 16 yrs. will be judged with adults); 2. beginners; 3. intermediates; 4. professionals. Pictures should be framed and wired for hanging. The exhibit will be judged by professional artists.

COST: A hanging fee of one dollar ($1.00) will be charged for each entry and fifty cents ($.50) for children under 16 yrs. with two entries per artist. (Space equirements have caused our limiting the entries to two this year, as just noted.)

HOW TO APPLY: Entry blanks will be mailed to former exhibitors and also may be obtained by writing to the addresses of the committee listed below. One half of the entry blank should be be submitted to me at the below listed address with your check prior to April 15, 1968. The other half should be attached to the picture. Make checks payable to Connecticut Physicians Art Association. Please fill in entry blanks completely so that entry can be categorized easily in the above four noted divisions.

SUBMITTING: Art works must be submitted to a representative of the Art Association in the lobby of the Hartford Hilton Hotel on Sunday, April 28th, between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. It may be possible to aid exhibitors with the transportation of art works by contacting members of the committee noted below. These art works must be picked up on Thursday, May 2, between 12 and 4 P.M. Members of the art committee or their representatives will be in attendance at the display throughout the exhibit at the state meeting. The Connecticut State Medical Society (nor the Art Association) can assume no responsibility for loss or damage of any cause to art works.

If further information is needed, the following persons may be contacted:

Stewart J. Petrie, M.D. President, 56 Minerva St., Derby, Conn.; Mrs. Orvan Hess, Vice President, 29 Old Orchard Rd., North Haven, Conn.; Edward Williams, M.D., 269 Church St., Naugatuck, Conn.; Charles O'Neill, M.D., 18 Asylum St., Hartford, Conn.; Herman Austrian, M.D., 935 White Plains Rd., Trumbull, Conn.; Donald Morrison, M.D., 26 Birch Rd., West Hartford, Conn.; Eugene Rightmyer, M.D., 114 Sherman Ave., New Haven, Conn.; Mrs. Jonathan Shoukimas, Chairman Art Committee Woman's Auxiliary; C.S.M.S., 26 Pheasant Hill Dr., West Hartford, Conn.

Artists — Attention!

Under no condition can art work be accepted after April 28th.

Other auxiliary members may be contacted if further information is needed:

Hartford County —

Mrs. Donald Morrison, 26 Birch Rd., West Hartford; Mrs. Merrill Rubinow, 68 Butternut Rd., Manchester

Middlesex County —

Mrs. Clarence Harwood, 1350 Old Mill Rd., Middletown

Windham County —

Mrs. Ralph Gilman, Willow Brook Rd., Storrs

New Haven County —

Mrs. Mark Hayes, 163 Ridgewood Ave., North Haven; Dr. John Hoffer, 153 Main St., Ansonia; Dr. James Mooney, 299 Seymour Ave., Derby

New London County —

Mrs. Clifford Wilson, 19 East Town St., Norwich; Mrs. James Harkins, 98 Case St., Norwichtown.

From the reports, comments and compliments received from the past years' shows, this seems to be a point of major interest of the annual meeting of the Connecticut State Medical Society. We therefore wish to thank the art hobbyists and encourage their continued participation in this exhibit.

Stewart J. Petrie, M.D., President
Connecticut Physicians Art Association

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ndications: For use in management of anxiety and tension occurring lone or as accompanying symptom complex to medical and surgical isorders and procedures. Though not a hypnotic, fosters normal eep through antianxiety and related muscle-relaxant properties.

Contraindications: History of sensitivity to meprobamate.

Important Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. (All tablets also available in REDIPAK® [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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Liver Scanning in Clinical Practice

Isaac Horowitz, M.D.

The examination of the liver with radioactive substances is a convenient and safe method in the differential diagnosis of liver disease. It renders reliable anatomic information regarding the position, size, and configuration of the organ and also indirectly provides information regarding liver function and its relation to space occupying masses in the abdomen. The test is based on the principle that liver cells selectively remove the major portion of certain radioactive substances from the circulating blood pool. The cells in the liver become radioactive and the emitted gamma photons are detected by a scintillation probe. The received impulses are transmitted to a light source which produces a photographic image—photoscan—or to a stylet which prints out the configuration of the organ in black dots or color dots—dot scan.[1,2]

In clinical practice the most commonly used compound is the colloid of gold Au 198. It is readily commercially available in convenient packaging and has an economical shelflife. After intravenous injection, 90% of the substance is removed from the blood and stored in the reticulo-endothelial cells of the liver and 10% is retained in the reticulo-endothelial cells of the spleen and bone. Colloidal gold has the advantage that it remains in the cells for a long time (half life 2.7 days). The scanning can be done at leisure at the most suitable time for patient and technician. Multiple views can be taken and it can be repeated after a 24 hour interval. If extrahepatic pathology is suspected, superimposed x-ray of the abdomen, lung scan, or kidney scan can measure the anatomical space between the liver and these organs. Significant uptake by the spleen and bone marrow are indicators of impaired liver function and advanced liver disease. The liver scan is helpful to mark on the skin the approach for an aimed liver biopsy.

Rose Bengal, labeled with Iodine 131, is the preferred substance in problem cases of jaundice. Rose Bengal is selectively absorbed by the polygonal liver cells, the same as bromsulphalein, and rapidly excreted into the biliary ducts, gallbladder and small bowel. The Rose Bengal concentration in the liver is continually changing as the dye enters and leaves. The thinner portions of the liver lose the dye very rapidly. Therefore, the anatomical borders are not as sharp as in the goldscan. The scan procedure has to be started within 30 minutes after injection. There is not enough time for repeat studies. Rose Bengal has the advantage of a low radiation dose to the liver.[3,4]

Radioactive Mat.	Dosage	Rad To Liver	Rad To Body	Study
Coll. Gold 198	1.5 μc/kg	3-5 Rad	.003 Rad	Liver
Rose Bengal ^{131}I	200 μc	.02 Rad	.001 Rad	Liver Function Biliary Duct System
G.I. Series Barium Enema	X-ray	4 Rad	3-7 Rad	

Discussion

For routine studies Radiogold is used. 150-200 microcuries are given intravenously. The scan is done about one hour after injection. Anterior and right lateral areas are scanned. The three dimensional information is essential for study. A series of marks are made on the skin to mark the midline and costal edges. The limitation of the test is that only lesions larger than 2.5 cm in diameter on the surface and larger ones within the liver can be readily recognized. Distortion of the liver contour can be caused by the heart, by an enlarged kidney, and a Riedel's Lobe. Eventration of the diaphragm, interposition of bowel loops, and marked scoliosis may change the position of the liver. Therefore, the x-rays of the abdomen, including G.I. studies should be correlated to avoid false conclusions due to anatomical variations.

The information gained is part of the liver profile which cannot be learned from routine radiological procedures or laboratory tests. The economy of the test is reasonable as compared to a battery of laboratory studies or x-ray studies. The safety of the test is considerable. The radiation dose is nominal and is smaller than sustained during various fluoroscopic and radiographic diagnostic procedures.

Hepatic scanning is useful: A. In the preoperative patient with known primary neoplasm to determine presence of liver metastases; B. In the evaluation of liver cirrhosis; C. In patients with space occupying masses in the upper abdomen out-

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DR. ISAAC HOROWITZ, Chairman, Department of Radiology, Park City Hospital, Bridgeport and Radiologist, Chief, Veterans Administration, Bridgeport Regional Office.

side the liver; D. In space occupying masses within the liver.

In the presence of jaundice, Rose Bengal ^{131}I can help differentiate between hepato-cellular jaundice and extrahepatic obstructive jaundice. (See Fig. 1-Fig. 4)

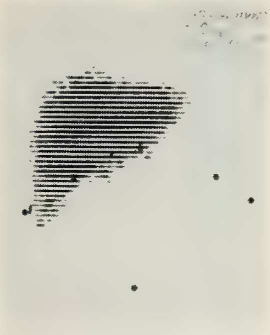

Fig. 1. Normal hepatic gold scan anterior view.

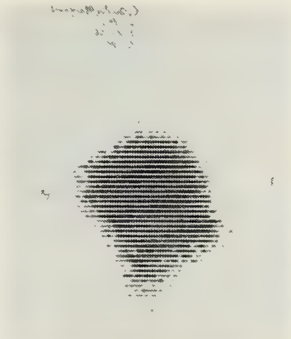

Fig. 2. Normal hepatic gold scan lateral view.

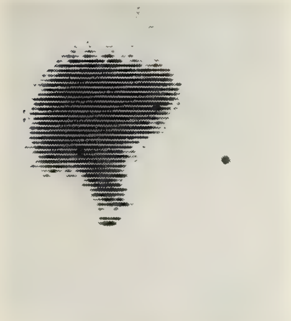

Fig. 3. Normal Rose Bengal scan showing liver and gall bladder.

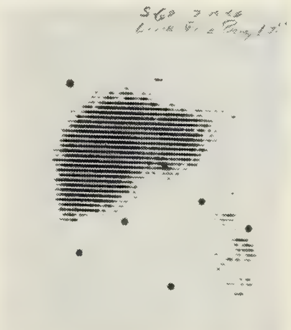

Fig. 4. Normal Rose Bengal liver scan at one hour. Radionuclide in liver, gall bladder and small bowel.

Discussion Of Cases

Two hundred consecutive liver scans were reviewed. 52% were scanned prior to surgery with a known primary neoplasm. 26% were evaluated for liver cirrhosis. 21% were scanned in the general workup for anemia, weakness, palpable abdominal masses, and jaundice. 1% were scanned for subphrenic abscesses or trauma to liver. In liver disease scans may become positive before chemical changes occur. A significant volume of hepatic destruction must be present before there is loss of liver function and the alkaline phosphatase or B.S.P. tests become positive.[5] In 104 patients with a known primary neoplasm the scan was positive for metastases in 24 patients. Some of the metastases were suspected; some were unknown. Most of the cases with positive scan of cirrhosis had liver biopsies. All biopsies correlated well with the scan diagnosis. In this series the cases with some loss of liver function and a normal scan apparently were not studied with a liver biopsy. We had no cases where the liver scan was normal and a liver biopsy showed changes of cirrhosis.

The scans in Fig. 5, 6, and 7 demonstrate the value of the test in the workup for malignancy prior to surgery. Case I. (Fig. 5 & 5A) A 64 year old female was admitted for ventral hernia. Preoperative workup showed an unsuspected small tumor in the right lesser pelvis. Liver scan showed an area of non function in the right lower liver wedge. Laparotomy revealed a carcinoma of the ovary with metastases to the liver, 4 cm x 6 cm, and a small amount of fluid in the abdominal cavity.

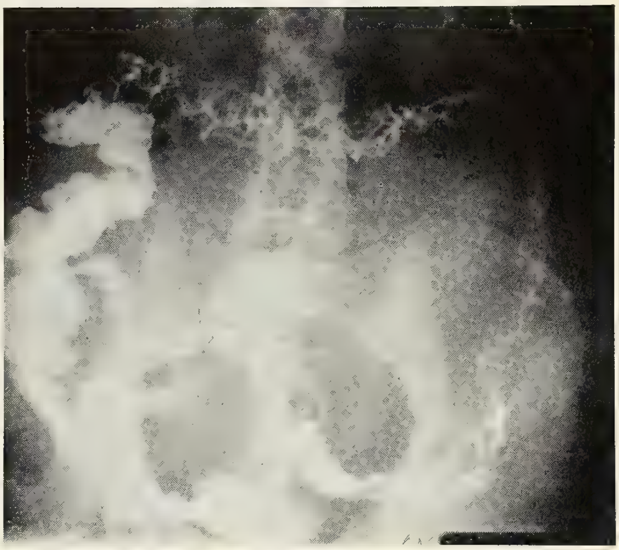

Figure 5

Case I: X-ray showing mass in right lesser pelvis not readily palpable because of the ventral hernia.

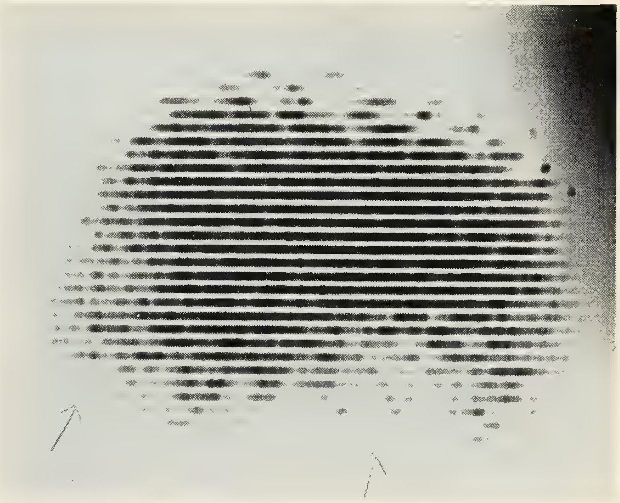

Figure 5A

Case I: Lateral gold scan showing defect at anterior inferior border of liver.

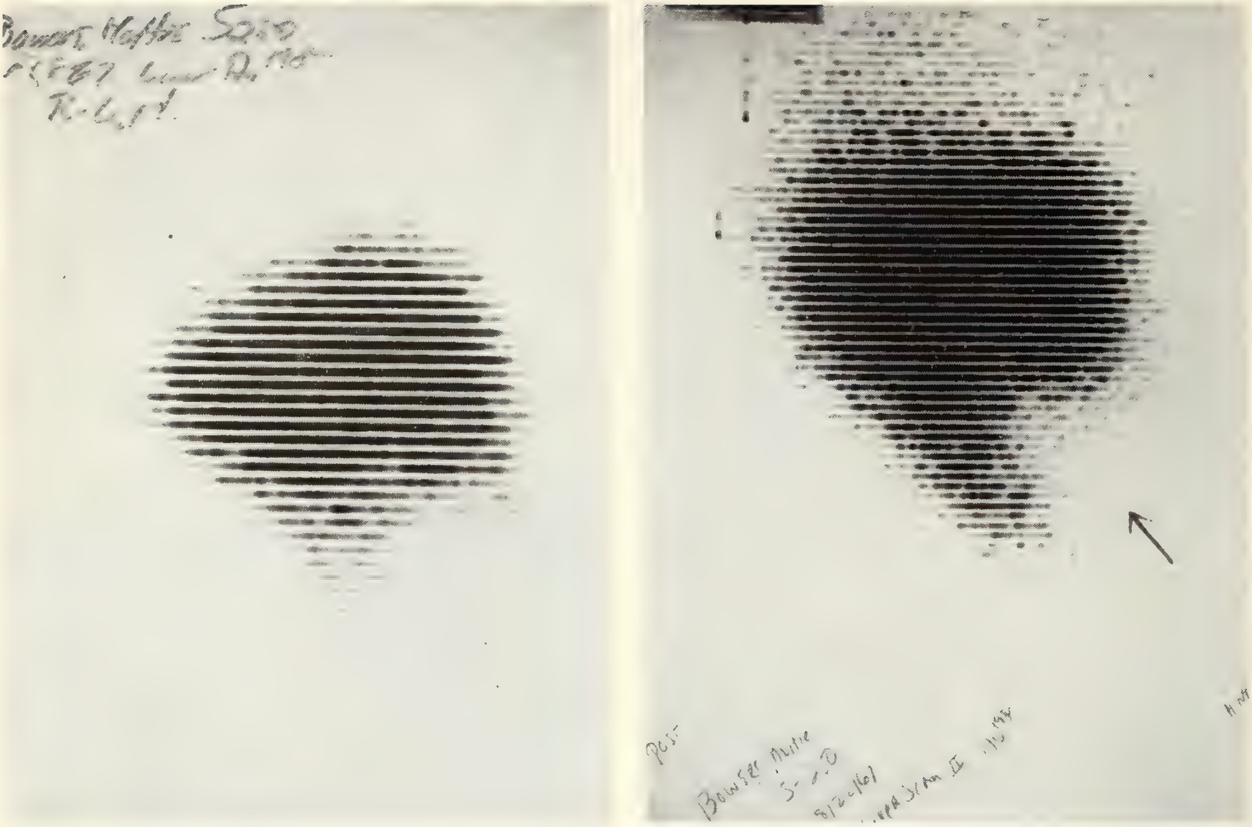

Figure 6 & 6A

Case II: Left: Laternal goldscan of liver. "Cold" defect at anterior inferior edge. Right: Lateral goldscan of liver. Eight months later the metastasis is larger and there is marked hepatomegaly.

Case II. (Fig. 6 & 6A) A 70 year old female admitted for study which revealed a carcinoma of the stomach. Liver tests were normal. Scan showed a defect in the liver. Gastrectomy was done. Surgeon could feel no pathology in the liver. Patient was readmitted after eight months. The repeat scan showed enlargement of the metastasis and hepatomegaly due to generalized metastatic spread in the liver and also radioactivity in the spleen.

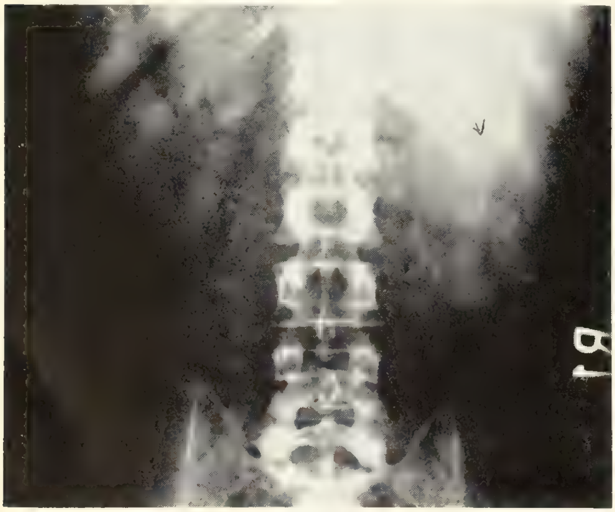

Figure 7

Case III: X-ray of abdomen with multiple small calcifications in liver.

Case III. (Fig. 7) A 54 year old male. Five years ago had radical surgery for carcinoma of rectosigmoid. On readmission the x-ray of the abdomen showed multpile calcifications in the right upper quadrant. Liver scan showed multiple defects consistent with multiple calcified metastases. Diagnosis was confirmed by biopsy, metastatic adenocarcinoma with calcifications. (Fig. 7A).

In all cases reviewed where the liver scan was negative prior to laparotomy, at surgery the liver was also found to be free of metastases by palpation. One case came to postmortem shortly after surgery. The liver histologically contained metastases which were not recognized by the scan or by the surgeon.

Large radioactive defects in the liver can be produced by a carcinoma of the gallbladder or by an inflammation of the gallbladder. Case IV and V had similar histories and similar liver scans.

Case IV. (Fig. 8) A 52 year old female admitted with right upper quadrant pain for three weeks. The liver profile was normal but the liver scan

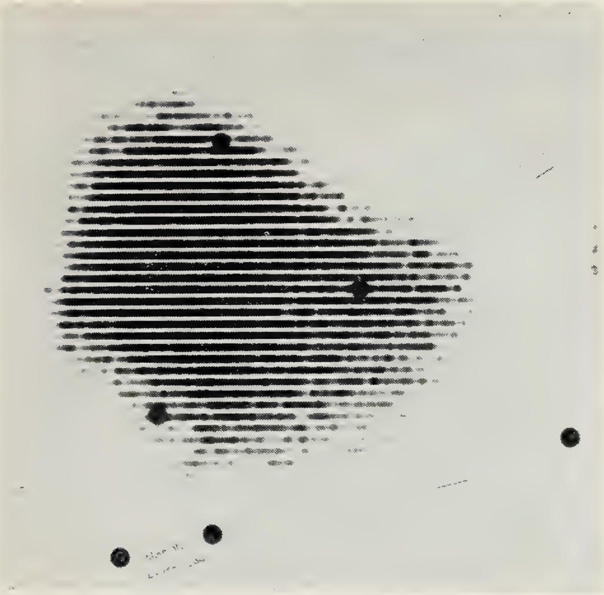

Figure 7A

Case III: Anterior scan with defect at lower border of liver.

showed a large defect. Liver biopsy showed chronic inflammatory disease. Laparotomy revealed carcinoma of the gallbladder.

Case V. (Fig. 9) A 65 year old male admitted with right upper quadrant pain. Eight months ago had prostatectomy for carcinoma of the prostate. Liver scan shows a large defect. Frozen section showed malignant cells. Cholecystectomy and removal of the mass proved it to be a large inflamed gallbladder.

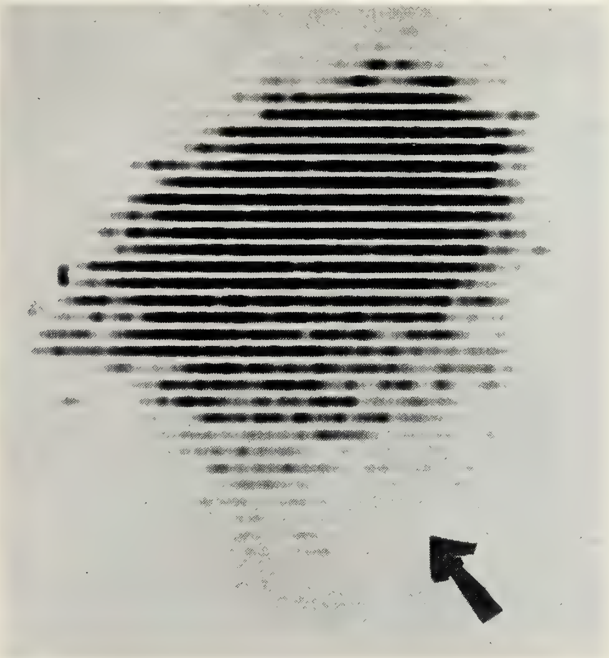

Figure 8

Case IV: Lateral scan showing defect at lower posterior liver edge. The lateral scan was more positive than the anterior scan. CA of gallbladder.

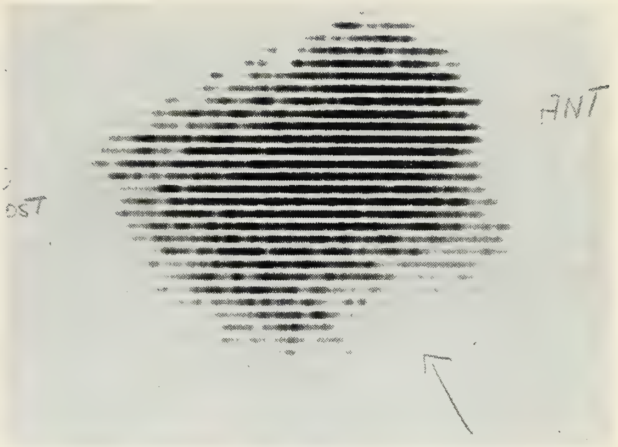

Figure 9

Case V: Lateral scan showing defect in liver. Inflammatory mas of gallbladder at surgery.

In patients with a history of alcoholism and a clinical diagnosis of cirrhosis, scans were found to show three following types of patterns.[7]

In the initial phase of minimal decrease in hepatic function, the scans can be normal. However, many of them show hepatomegaly or marked hilar fullness. There is no radioactivity in the spleen or bone marrow. The presumptive positive scan findings of hepatomegaly which showed fatty infiltration correlated well with the liver biopsies.

In the phase with moderate decrease in hepatic function, the liver is patchy. There is significant uptake of radiogold in the spleen and bone marrow. On the scan the contour of the liver, bone marrow and spleen fuse together to form a characteristic silhouette. All liver biopsies were positive for portal cirrhosis.

In the far advanced phase with marked loss of hepatic function, the liver is very small and patchy. The spleen is intensely active. The major portion of the isotope is phagocytized by the spleen and bone marrow. The patient may show signs of jaundice, ascites, and G.I. bleeding. Some are candidates for splenoportal shunt operations. The scan changes in cirrhosis are said to be due to arteriovenous anastomoses and reduced blood perfusion of the liver. The up-take by the bone marrow is rather typical for alcoholic cirrhosis.

Case VI. (Fig. 10) A 47 year old female admitted with history of alcoholism, weight loss, and right upper quadrant pain. The B.S.P. was 7.5%. Other liver tests were negative. The liver scan showed hepatomegaly. Liver biopsy was positive for fatty infiltration.

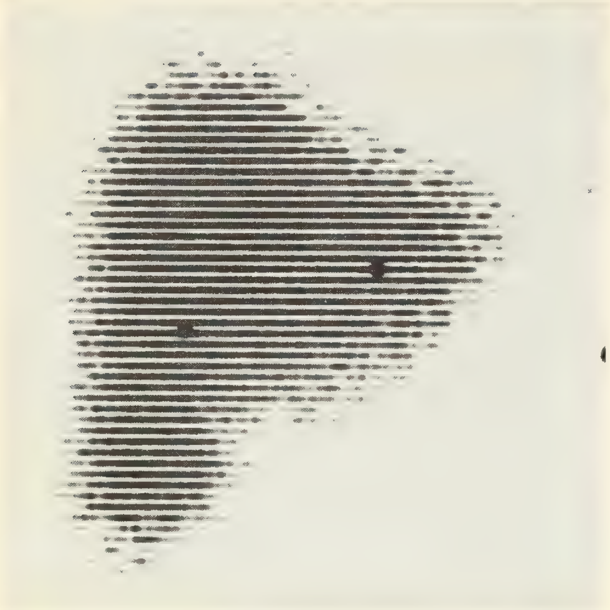

Figure 10
Case V: Anterior goldscan shows marked hepatomegaly. Black dots mark costal margins.

Case VII. (Fig. 11) A 50 year old female admitted with a ten year history of alcoholism, cirrhosis, hepatomegaly, and jaundice. Liver tests showed marked decrease in hepatic function. Liver scan was typical of cirrhosis with radioactivity in the liver, bone marrow and spleen. Liver biopsy was positive for cirrhosis. Liver tests and jaundice improved under therapy.

Case VIII. (Fig. 12) A 56 year old male admitted with melena, hematemesis, known cirrhotic. Lab tests showed marked loss in hepatic function. Liver scan typical of cirrhosis, far advanced. Workup revealed marked portal hypertension and he was referred for splenoportal shunt operation.

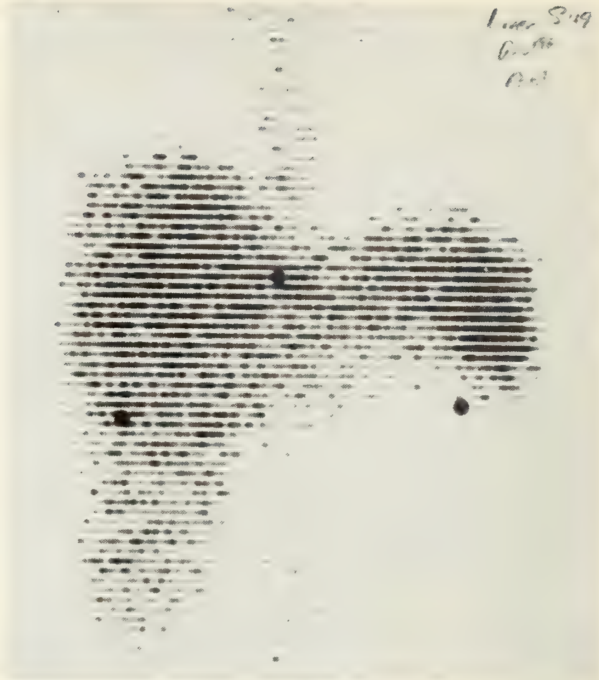

Figure 11
Case VII: Anterior goldscan. Marked radioactivity in a patchy liver, bone marrow and spleen. Butterfly silhouette.

The liver scan in postnecrotic cirrhosis due to infectious hepatitis has similar pattern as seen in advanced Laennec cirrhosis. Case IX. (Fig. 13) A 54 year old female educator admitted with bouts of swelling of feet and diarrhea with no history of alcoholism. She had intolerance to liquor. Liver profile was highly positive. Bilirubin 2.3 mg%, thymol 9U, B.S.P. 41% retention. Liver scan was positive for cirrhotic pattern. Liver biopsy showed postnecrotic cirrhosis. After the scan, a history of hepatitis 15 years ago was obtained.

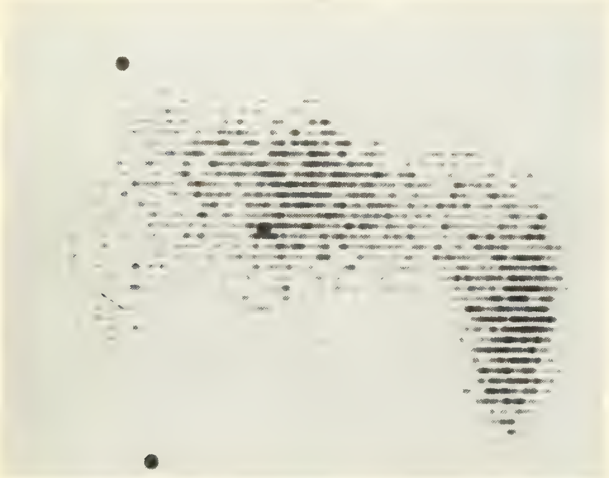

Figure 12
Case VIII: Anterior goldscan. Liver barely outlined. Most of the radionuclide is retained in the bone marrow and spleen. Typical for far advanced cirrhosis.

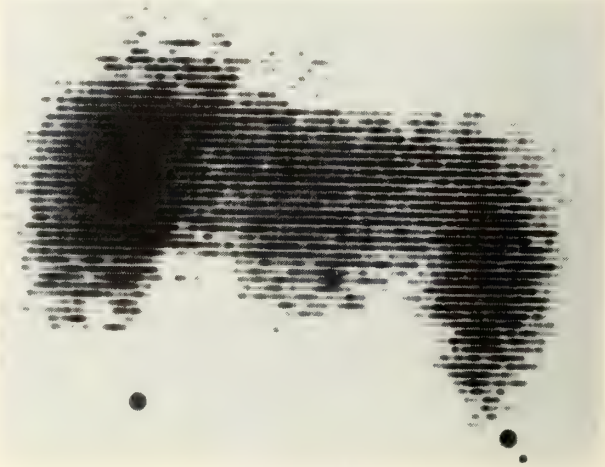

Figure 13
Case IX: Anterior goldscan. Post hepatitis cirrhotic liver. Marked activity in bone marrow and spleen.

In space occupying lesion in the abdomen, the goldscan defines the contour of the liver and the palpable mass can be marked with black dots on the scan. Case X. (Fig. 14) Eighty year old woman admitted with palpable mass in abdomen. The liver scan revealed that the mass was separate from the liver. Laparotomy identified the mass as a retroperitoneal tumor, a giant follicular adenoma.

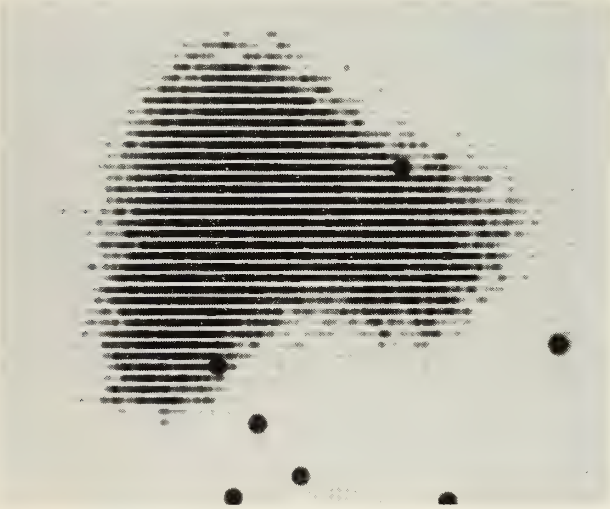

Figure 14

Case X: Anterior goldscan showing normal outline of liver. Black dots mark the palpable abdominal mass.

In lesions located under the diaphragm, the liver scan identifies the relation of the mass to the liver. Case XI. (Fig. 15 & 15A) Sixty year old female was evaluated for a diagnosis of mass in upper abdomen.[5] There was a history of fever, chills, and right upper quadrant pain over a six week period. The x-rays showed a large right upper quadrant mass and an air fluid level under the diaphragm and a diagnosis of subdiaphragmatic abscess was made. The liver scan was positive for a space occupying mass between diaphragm and right lobe of liver. Laparotomy confirmed the diagnosis of a neoplastic liver abscess secondary to a carcinoma of the ovary.

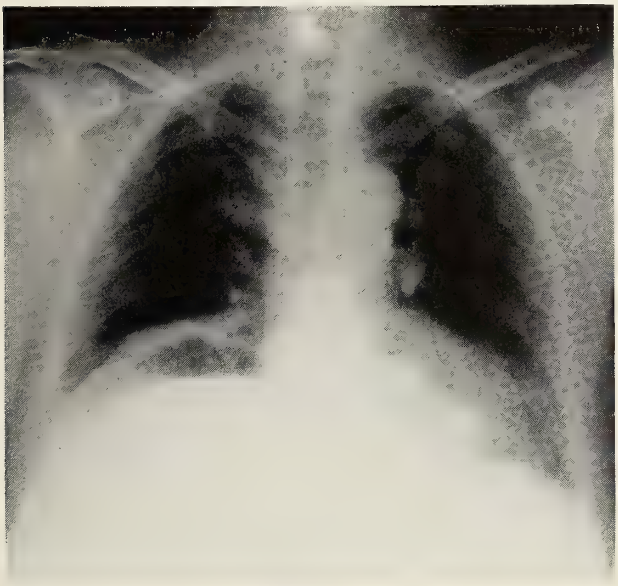

Figure 15

Case XI: X-ray showing air fluid level under elevated right diaphragm.

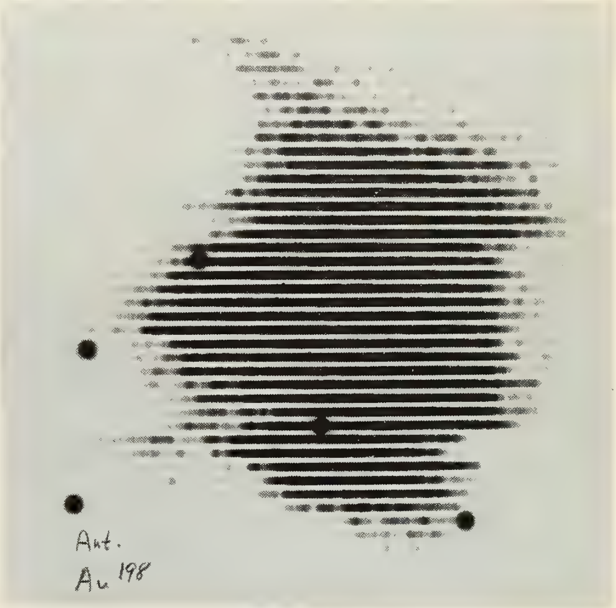

Figure 15A

Case XI: Anterior liver scan showing obliteration of the diaphragmatic contour of right liver lobe and displacement of the liver inferiorly and medially. Superimposition of x-ray localizes abscess.

In scanning not everything is black and white, there are some gray areas. Hepatomegaly is encountered in many clinical diseases. In hepatomegaly due to carcinomatosis, hyperthyroidism, chronic inflammatory disease and chronic heart disease there is often marked radioactivity in the spleen as is observed in cirrhosis. Deep seated lesions in the liver are difficult to recognize.

In problem cases of jaundice radio Rose Bengal scans have diagnostic usefulness.[6] Rose Bengal has been known to be a sensitive liver function test. Lugol solution is given the night prior to scanning to block the thyroid. Twenty minutes after intravenous administration of 200 microcuries of Rose Bengal ^{131}I, the scan is started. A normal Rose Bengal scan will outline liver, small bowel and at times the gallbladder. (See Figure 4) If these organs are not seen on the scan a followup scan will solve the problem whether the obstruction is complete or partial. In complete extrahepatic obstruction, where a localized stone or tumor produces compression of the common duct, the diagnosis is very accurate. In jaundice due to hepatitis the scan diagnosis is very helpful because radioactivity is seen in the liver and in the small bowel. In partial obstruction or in partial obstruction associated with marked decrease in hepatic function, the scan findings are of equivocal value. Radiosotope liver function studies and blood clearance studies are still performed as part of the study but in my experience the results make no significant contribution to a definitive diagnosis.

Case XII. (Fig. 16) A 24 year old female with right upper quadrant pain and jaundice. Bilirubin 19 mg%, Rose Bengal scan showed a patchy liver and radioactivity in small bowel. Scan diagnosis of hepatocellular disease was confirmed by biopsy. In the recovery phase, the liver scan returned to normal.

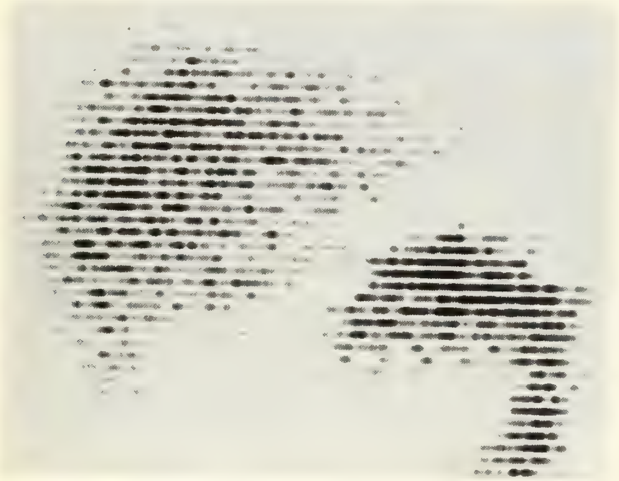

Figure 16

Case XII: Anterior Rose Bengal scan. Patchy liver and radionuclide in small bowel. Patient with infectious hepatitis.

In complete extrahepatic obstructive jaundice, dye is seen in the liver but none in the small bowel. At 24 hours, radioactivity may be present in the kidney and bladder and must not be confused with activity in the bowel. In extrahepatic obstruction, the common duct and biliary ducts can sometimes be recognized as increased or decreased radioactive defects. Case XIII. (Fig. 17) A 75 year old female admitted with a history of 20 pound weight loss, jaundice, light stools, and dark urine. Rose Bengal scan positive for extrahepatic obstruction. No radioactivity in the small bowel at 2 and 24 hours. Laparotomy showed inflammatory obstruction at the sphincter of Oddi. In one case of hepatocellular jaundice due to prolonged thorazine intake, the Rose Bengal scan showed a small, patchy liver and no dye in the small bowel. A repeat scan 4 weeks later was normal.

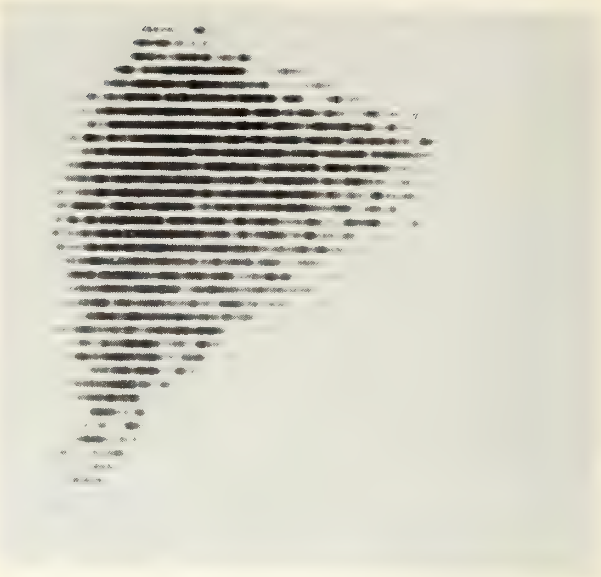

Figure 17

Case XIII: Anterior Rose Bengal scan. Normal outline of liver. No radioactivity in common duct or small bowel. Extrahepatic obstruction at sphincter of Oddi.

Summary

A nonselected series of 200 patients recently examined by liver scanning have been reviewed. The liver scan with radioactive material adds a simple approach to study the liver. It gives useful information in the delineation of primary tumors, metastatic tumors, cirrhosis or extrahepatic pathology. In the differential diagnosis of jaundice, the Rose Bengal scan is helpful to determine extrahepatic obstruction or hepatocellular jaundice.

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Some Observations Concerning Efficiency in the Psychiatric Clinic

T. P. Millar, M.D.

Introduction:

We in psychiatry are in the midst of a revolution in patient care. The treatment of the psychiatric patient is being returned from the State hospitals to the resources of his community. The outpatient psychiatric clinic has been the principal such resource.

Since 1940 there has been a proliferation of outpatient psychiatric clinics, and it is now a fact that the general hospitals accept more psychiatric first admissions than do the public mental hospitals.[9] Furthermore, the outpatient psychiatric clinic is expanding to become the Community Mental Health Center.

The pattern of operation of these new clinics and centers will be, in many cases, derived from that of the traditional psychiatric clinic. To the extent that this has been an effective pattern, patient care will be well served.

The *efficacy* of the psychiatric clinic has been subject to considerable examination in the literature. It has been suggested, for example, that the clinic does not always address itself to the mental health of those whose needs are greatest.[7] Some have felt that the clinic has become rigid, that the roles and procedures such as intake have become inflexible to the detriment of patient care.[6 3 10] There is concern that the clinic is not keeping pace, not developing imaginative new approaches or re-examining codified theory.[6] The effectiveness of treatment procedures has been questioned.[6 2 13] Quality of care is an elusive, difficult thing to measure, and while crucial, is not the primary concern of this paper.

The *efficiency* of the psychiatric clinic has been subject to less examination. There has been little discussion, for example, of cost-of-service or how this is distributed. There are few articles concerning utilization of staff time. There is not a great deal to guide the psychiatrist who must administer the burgeoning new programmes. In many relevant areas, guidelines are yet to be established. These will probably have to evolve from ongoing exchange of experience amongst those presently dealing with these problems.

This paper seeks to report some experience in these areas, experience derived from several years contact with various clinics as a consultant psychiatrist, and a more brief experience as a director undertaking to reorganize a clinic.

Cost-of-Care

It would seem reasonable that a cost-of-care index might well provide Directors, Board members and those responsible on a state and federal level for the administration of operating funds, with a useful measure of the efficiency of the clinic. The needed figures are not readily available, nor have precise formulas for establishing cost of care been publicized.

It seems reasonable that a rough, but useful indication of cost-of-care might be obtained by dividing the operating budget of the clinic by its product, measured in relevant units. The operating cost would be the total budget for the period involved, unless of course that budget included some special or unusual expenditure such as a major building cost, which should probably be distributed over several years.

The product of the outpatient psychiatric clinic includes:

- Evaluation and treatment of patients
- Consultations and conferences with community agencies
- Training and public educational activities
- Research

The useful unit for quantifying such product would appear to be hours spent in each of these activities. The State of Connecticut keeps figures of clinic product broken down in such terms.[5]

If one utilizes the following formula, one arrives at a cost-of-care per hour of clinic product.

$$\text{COST-OF-CARE} = \frac{\text{Total Operating Cost}}{\text{Product in Hours}}$$

DR. T. P. MILLAR, Attending staff of the Sharon Hospital, Sharon, Connecticut.

Utilizing this formula, the author was able, using figures available to him, to derive cost-of-care estimates for two clinics. These were:

Clinic A $23/hr.
Clinic B $32/hr.

Naively perhaps, the author was surprised at these costs.* It is evident that these costs are as high as, or higher than the cost of private psychiatric care.** If one remembers that a considerable portion of product hours are provided by social workers or psychologists, who are paid considerably less than the psychiatrist, one is led to wonder why these costs are so high.

The Utilization of Staff Time

One of the obvious questions that arises is: What proportion of the working hours of the professional staff is actually utilized in clinic product, in treating or evaluating patients, consulting to the community, training, public education and research?

Once again, such date is not easily obtained, nor necessarily accurate. There is a tendency, for example, to lump together activities designated as "on behalf of the patient" with direct service to the patient. These activities include telephone calls, dictation etc. In general, the author has found estimates of staff utilization to be unreliable.

Examining such matters in a particular clinical situation the author was impressed that deficient utilization of professional staff time was a major determinant of high product cost. The staff estimate of their productivity was in excess of 24 hours of the work week, but a review of the records revealed that something under 16 hours per week, per full time staff member had actually been spent in those activities designated clinic product.

In order to evaluate the productivity of his staff, the clinic director needs some standard. Such can be empirically derived, i.e., what is going on in other clinics? How do my staff measure up to local, state or national standards? Once again, figures are not readily available. In a recent workshop at Orthopsychiatry annual meeting[1] it was reported that "in some parts of the country it has been found that only 30% to 35% of staff time is devoted to direct service."

Because such figures were not available the author endeavored, using published statistical tables,[5] to arrive at useful estimates of staff utilization for the 45 outpatient psychiatric clinics in Connecticut. Certain difficulties were encountered, and these will be described. They do not, in the author's opinion, render the determinations invalid, although they do tend to introduce some error in the direction of overestimating staff utilization.

The principal measure of clinic product reported for each clinic is that of "Staff interviews with or about patients" for the year in question. This is a staff interview count, not hours spent with patients. Equating each staff interview with an hour is to introduce error, most marked in those clinics where patients are seen briefly for support or drug therapy. In such cases staff utilization appears excessively high. Since interviews rarely last more than an hour, the opposite error is unlikely.†

To this figure of staff interview was added "group session" interviews, and "professional man hours in community service activities". These included all of the activities mentioned as part of clinic product earlier in the paper, apart from research, which consumed negligible amount of staff time in most of the settings in question.

From these determinations a figure of clinic product, in hours, was obtained for each of the 45 clinics, for the various types of clinics, and for the state as a whole.

These clinic product figures were then divided by the "professional staff hours on duty" as reported for each clinic. Since these "professional staff hours on duty" are actual hours on duty and do not include holidays, sick time etc. they are smaller numbers than might be obtained by estimate. The clinic product hours, as previously determined, would therefore appear as a larger fraction, and staff utilization percentages will be raised by a small and probably constant figure.

Despite these errors, both of which would tend to report erroneously high staff utilization percentages, quite low figures result from these calculations.

For the State of Connecticut, the following results obtain. There were, in 1964, approximately 125,000 staff interviews with or about patients conducted by the professional staffs of all clinics. The clinics devoted approximately 20,000 professional man hours to community service. The total product is therefore, 145,000 hours. Professional staff hours on duty totalled 340,000 during the year. The staff utilization percentage is therefore a maximum of 43%.

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* The author has been assured informally by knowledgeable colleagues that these figures are not particularly out of line.

** The question comes up, as it did in a recent workshop[1] as to whether it would not be less expensive for communities to underwrite the private care of the psychiatric patient. This is a complex subject, beyond the scope of this paper.

† There might be point in breaking staff interviews down into ¼, ½ and 1 hour categories to facilitate studies of productivity.

For the 45 clinics similar figures can be obtained. Utilization percentages vary widely from clinic to clinic, and it seems likely that brief interviews are, at least partially responsible for the high (average 90%) figures found for the State Hospital Clinics. Among the General Hospital Clinics figures range from 25% staff utilization to 75% utilization, for an average of 42%. For the Child Guidance Clinics, where there is probably the greatest correspondence between staff interviews and actual hours, the lowest figures were seen. The figures were mostly in the 20% to 40% range and the average was 34%.

Such utilization figures seem, to the author, to be low. Amongst clinics doing similar work, quite wide disparities in utilization are seen, so it is apparent that varations related to the efficiency of individual clinics are part of this picture. It would seem unwise to accept them uncritically as standards of expectation from the professional staff.

How then, to determine what is a reasonable expectation of a staff member in an outpatient psychiatric clinic?

The literature is sparse. The author found direct communication with other clinic directors and mental health professionals produced illuminating opinions concerning these matters.[11] [12] It was pointed out that for social workers, the skill level of the individual worker, the orientation of the program and its administrative structure, had a bearing upon what one might expect. It was also pointed out that to lay down quantitative expectations was to risk freezing personnel utilization into rigid staffpatient ratios. Despite these reservations, the general concensus seemed to be that it would not be unreasonable to expect that over half of the hours of the workweek might be expected to be utilized in "direct patient care."

In the clinical situation with which the author was dealing the following guidelines were utilized. They are reported here in the hope that they will stimulate some exchange of experience concerning these increasingly important matters.

A baseline expectation of 25 product hours per week, per full time staff member, was established. The way in which these hours were spent varied, depending upon the particular clinical activities of particular staff members. The psychologist, for example might spend several hours per week in research activity, which, incidentally he was pleased to have raised to the status of product and to have time allotted for. Another staff member might be involved in consultation for part of this time.

The 25 hour expectancy was diminished, hour for hour, to allow for administrative, supervisory or other non-product responsibilities. For new staff the expectancy was reduced during their first few months of employment. The expectancy was considered a minimal one; there was no prohibition with respect to exceeding this baseline. It was felt that the remaining time was ample for conferencing, record keeping, telephone calls and incidental clinic business.

The responsibility for scheduling himself to reach this output remained with the individual staff members who, to this end, maintained their own appointment books.

Causes of Diminished Utilization of Staff Time

Returning to the general subject of impaired efficiency in the psychiatric clinic, some aspects of this problem, as it presented itself in a particular situation will be discussed, and, in the case of missed appointments, the way in which the problem was handled will be described.

There are a number of ways in which staff time can be dissipated unproductively. Among these are: cancelled or failed appointments, excessive conferencing, inappropriately thorough record keeping and redundant or unnecessary supervision.

1. Patient Cancellations:

In the clinic in question, missed appointments for the previous year had amounted to 19% of the appointments made. Because of the magnitude of the problem, a study of it was initiated and policies intended to deal with the problem were instituted. After 4 months appointments missed had diminished to 9% at which figure they remained fairly constant. The policies initiated were as follows.

When a patient called to cancel his appointment he was, whenever possible, put through to his therapist. When the therapist was busy, the secretary informed the patient that his therapist would be calling him concerning the appointment. The patients soon learned that cancelling an appointment involved a telephone confrontation with their therapist. Where the avoidance of contact was a relevant determinant of the cancellation, this route to such avoidance became ineffective and the patients began to utilize it less.

Failed appointments, that is when the patient did not show up for his appointment nor call to cancel, were dealt with directly. The patient was informed that further appointments could not be held for him if he failed to come. The issue of therapy and his part in it was dealt with directly. In some cases this led to termination of what had become a desultory and unproductive relationship. In others it led to the resolution of a treatment impasse.

A weekly table of cancellations and failures kept the staff aware of the problem and brought repeated cancellations by the same patient to the attention of the supervisor, who was then in a position to help the therapist with these.

In each case, the reason given by the patient for his cancellation was written down. It just did not seem possible, as the data accumulated, that our patients' cars could be subject to that much malfunction, or their children to that much unheralded illness. A certain developing skepticism in the staff may have been communicated to their patients, which, if it did not produce better attendance, at least resulted in more imaginative excuses.

The secretarial staff were encouraged to fill cancelled appointments whenever possible. To this end non-emergent appointment requests were not filled immediately but were kept open, pending cancellations.

Finally, the therapists were expected to schedule 2 to 3 extra hours per week, i.e. 27 hours with the expectation of netting 25 hours, to allow for the unavoidable missed appointments.

As has been mentioned, these policies and perhaps the attention focussed upon the problem, led to a significant reduction in missed appointments and an improved utilization of staff time. It also led to some impressions about missed appointments.

It is well known that missed appointments, particularly failed appointments, may represent problems in treatment. In the initial phases of treatment, missed appointments may represent the maneuvers of the patient as he determines for himself the dimensions of the treatment contract. In later phases they may represent plateaus, or impasses in treatment. Such are amenable to supervisory assistance, and therapists can become more aware of their part in the cancellations problem and thoughtful about it.

Lower class patients tend to miss more appointments than middle class patients. This may be, as has been suggested, because they are inclined to lead unscheduled lives. There may be other factors involved. For many such patients, treatment is seen as involving something concrete being done to them. The good medicine combats the bad within. The "talking therapies" for these patients may seem to be "doing nothing". Their life style is one of acting, one in which verbal communication plays a minimal role. Missing appointments for such patients may be an indication that the treatment process is not meaningful as his symptoms subside, or his crisis is resolved.

The 1964 Connecticut statistics[5] commenting on cases that had been treated, draw attention to the fact that almost half of the patients withdrew from treatment. Of these withdrawing patients, 60% did not notify the clinic. How much staff time was lost in failed or cancelled appointments before these patients were terminated can only be guessed at. It is the author's impression that such patients account for a very large percentage of missed appointments.

One remedy instituted, when these patients were discovered in the supervisory sessions, was to place them on p.r.n. clinic contacts, rather than regular appointments. For some of the staff, this represented a concession to the patients limitations in motivation. Pointing to the patients obvious personality problems and the likelihood of further adjustment problems, the staff was concerned that the job was less than done.

It was the author's view that the problem lay as much with what the clinic had to offer as with what the patient was able to accept. Perhaps in continuing to offer the patient psychotherapy when it was proving ineffective, we do so because we don't know what else to do to help him change. Perhaps we are like the doctor whose patient needs Streptomycin (or some yet to be devised remedy) but continues to receive Penicillin, because that is all the doctor has. Would it not be better to save the Penicillin for the patient who can benefit from it, and face up to the need for a new remedy?

While missed appointments will undoubtedly always be with us, their impact upon utilization of professional time in the clinic can be minimized. This is a problem responsive to sound administration and a clear responsibility of the clinic director.

2. Staff Conferences:

If a football team spends too long in the huddle, somebody blows a whistle. It is time, perhaps, that somebody blew the whistle on the psychiatric team.

For some, the conference has become the sine qua non of clinic function. Historically the conference arose out of the need for the three disciplines, with their basically different information viewed from different theoretical bases, to pool that information in order to plan more effective intervention for the patient. Today, the three disciplines bring very similar information to the conference, and, in many cases, approach their data from a similar, if not identical, theoretical base. The team conference today, while interesting and perhaps reassuring, may not always be necessary.

Staff conferences are expensive of professional time; one hour per professional staff member present, per hour of conference. This is particularly inefficient in the large clinic. It seems evident that no more staff conferences than are necessary should be held, that these should involve only the necessary persons and that they should not last longer than required for the business at hand.

Some conferences may be unnecessary. The 'intake conference' for example may be rendered unnecessary, or at least its length and number of participants significantly reduced. If, as Maholick[9] has advocated, the psychiatrist sees the patient first and then utilizes the skills of the other members of the team, as necessary, not only will professional time be saved, but also, the need for intake conferencing will diminish.

It may be said that just as there is a clinging to conventional roles in the clinic, so is there a reluctance to give up institutions such as the conference. A careful examination, in the light of new clinic roles and pattern may reveal that a given conference has lost its purpose and may be abandoned.

One purpose of the staff conference which should not be lost sight of, in the pursuit of efficiency, is the part it plays in the maintainance of staff morale. The mental health professional, be he psychiatrist, psychologist or social worker, needs to feel he is not alone, that he is part of a group of professionals whom he values and who value him. His work places him in a situation where self doubt, uncertainty and discouragement can easily arise. He will make mistakes. Even when he does not make mistakes, he will not be able to help some of his patients. He may find, in the sharing of the staff conference, a sense of group identity and support. In the discussions of theory and practice that take place in a conference he may find something that serves to make sense of what has seemed a welter of confusion and blind groping. A regular, general staff conference is probably a necessary experience if group identity and morale are to be sustained.

3. Record Keeping

A great deal of dictation is done in the psychiatric clinic, some of which may be unnecessary.

It seems reasonable that a comprehensive psychiatric report eventuate from each evaluation so that a report may be sent to another agency concerning the patient and it will not be necessary for that agency to duplicate the expenditure of staff time. Treatment notes should be brief. Process recording is for the training experience. The purpose of dictating is not to justify ourselves to those who follow, nor is it to get our thoughts on paper where we may examine them at our leisure. It is to record the salient aspects of what went on in the treatment of the patient.

4. Supervision

Staff time spent in supervision is time lost to patient care for both supervisor and supervisee. Insofar as this controls the quality of care, its contribution to *efficacy* in the clinic is considerable. However, as professional competence develops, the need for supervision should diminish. For very experienced workers it may be the p.r.n. supervision is sufficient. The duplication of supervision to avoid interdisciplinary jurisdictional disputes is particularly wasteful.

Efficiency and the Direction of the Psychiatric Clinic

Efficiency in the psychiatric clinic is a concern of all of the staff, but it is the responsibility of the clinic director. Directing the psychiatric clinic is a particularly complex task. The need and supply being what they are, it is often the case that young men, fresh from their training become directors of clinics. Psychiatric training addresses itself but minimally to administrative concerns, so these men are often uncertain and sometimes inclined to abrogate their authority.

It is sometimes said that physicians make poor administrators, but it seems unlikely that this need be true. Administrative skills can be acquired. Perhaps if, in the course of his psychiatric residency, the trainee was given some responsibility for the administration of a fragment of the training institution, as well as some basic information, his interest in and capacity for administration might be nurtured.

In order for the director to administer his clinic well, the lines of authority and responsibility need to be delineated with clarity. As James[7] puts it; "One of the chronic problems in organizations with a high proportion of professionals is the continuous pressure to reduce administrative controls on professional discretion." He goes on to describe the process by which line authority is eroded and the direction of the system deflected from its purpose, patient care, to the maintenance of staff vested interests. At a time when roles of the various professionals, as determined by their training, are undergoing much change, this erosion may sometimes be aggravated by the status concerns of the involved individuals. The process is a subtle one, ill understood by all parties to it. It is a most difficult thing for an inexperienced director to detect and understand.

It is not surprising if the new director, facing these complexities, chooses to spend his time doing what he feels reasonably capable of doing, be it patient care or public relations, leaving administrative responsibilities to others. In a penetrating paper, Eiduson[6] has pointed to other roots of the tendency amongst clinic directors to abrogate their authority and to rationalize this abrogation as a democratic sharing of responsibility.

The point is that, with poor direction, the psychiatric clinic loses its orientation to patient care. As an organization maintaining the interests of its staff it may be highly efficient, but as a treatment program it will begin to demonstrate the kind of inefficiency to which attention has been drawn in this paper.

The clinic director who exercises his authority responsibly, determines the pattern of function of the clinic, taking as his primary guide, the needs of the patients who present themselves for care. He utilizes the specific competences of his staff toward the goal of effective treatment. To do this he must know what those specific competences are, and he must have continuous information as to the effectiveness of the procedures involved. He must know what is going on in his clinic and measure its effectiveness against some external standard.

One of the difficulties amenable to solution, with what we have at hand, is that of informational feedback. The problem solving capacities of the administrative organism, in this case the psychiatric clinic, depend upon its ability to use the results of its actions as part of the information upon which subsequent action is determined. If for example, the directors of outpatient psychiatric clinics were regularly provided with feedback consisting of *comparative efficiency reports* based on determinations of utilization of staff time and cost-of-care, it is possible that some changes in their subsequent actions would eventuate. If the Board's Members received such information, it is possible that they would be able to effect changes in the organization which would have a salutary effect upon its efficiency. It is by a series of recorrected actions that the psychiatric clinic, like other organizations, can come to match its performance to standards of care.[7]

Addressing itself to the problem of improving administration in the psychiatric clinic, the Connecticut Association for Mental Health[4] recommended that the Department of Mental Health set itself the task of establishing guidelines for the administration of clinics receiving aid from it. It suggested the wide circulation of *comparative statistics,* periodic meetings to consider the implications of the statistics, and even the withholding of grants. It also recommended an active program of skilled consultation to clinics on matters of administration and programming. It seems likely, indeed that such actions are exactly the kind of informational feedback needed. State bodies administering funds for psychiatric clinics are peculiarly able to provide this feedback, for they have the comparative figures.

Summary

This paper seeks to examine aspects of efficiency of the outpatient psychiatric clinic. It suggests that cost-of-care figures for such operations are calculable and reveal that the cost of psychiatric care in the clinic is as high as or higher than private psychiatric care. Inefficient utilization of professional staff time is reported to be a contributing factor to high cost of care. Factors contributing to inefficient utilization of staff time are seen to be missed appointments, excessive conferencing, record keeping and supervision. Guidelines for staff expectancies are offered. The role of the clinic director in these matters is explored and some recommendations for increased feedback of data regarding comparative cost of care and staff utilization are made.

Part of concern for efficiency in the psychiatric clinic arises out of the marked expansion of such facilities presently under way. This nation is spending more money for mental health than it has ever done. The perpetuation of inefficient patterns of

care can only lead to waste. It is clearly the responsibility of the mental health professional to make sure this money is not wasted, that it buys all the effective patient care possible.

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PRAYER OF MAIMONIDES

I begin once more my daily work. Be thou with me, Almighty Father of Mercy, in all my efforts to heal the sick. For without thee, man is but a helpless creature. Grant that I may be filled with love for my art and for my fellow-men. May the thirst for gain and the desire for fame be far from my heart. For these are the enemies of pity and the ministers of hate. Grant that I may be able to devote myself, body and soul to thy children who suffer from pain.

Preserve my strength, that I may be able to restore the strength of the rich and the poor, the good and the bad, the friend and the foe. Let me see in the sufferer the man alone. When wiser men teach me, let me be humble to learn; for the mind of man is so puny, and the art of healing is so vast. But when fools are ready to advise me or to find fault with me, let me not listen to their folly. Let me be intent upon one thing, O Father of Mercy, to be always merciful to thy suffering children.

May there never rise in me the notion that I know enough, but give me the strength and leisure and zeal to enlarge my knowledge. Our work is great, and the mind of man presses forward forever. Thou hast chosen me in thy grace, to watch over the life and death of thy creatures. I am about to fulfill my duties. Guide me in this immense work so that it may be of avail.

May Emotional Reactions be Precipitated by Allergens?

Marshall Mandell, M.D. and Gilbert J. Rose, M.D.

May emotional reactions be precipitated by allergens? A number of difficulties stand in the way of a simple answer. First, though the clinical experience reported here may be suggestive, the few experimental challenges are methodologically insufficient. Likewise, the double-blind procedure does not eliminate the complexities in studying an individual's subjective reactions to a given stimulus, for as soon as an agent provokes a somatic cue the subject is no longer "blind." Finally, it is never possible to exclude completely the effects of an investigator's theoretical expectations and, most important, the conscious and unconscious aspects of the psychological climate between doctor and patient may influence the results considerably.

Nevertheless, our findings suggest that allergens may be included among the stimuli which may provoke emotional reactions. This may be significant because a recent review of the literature contained no reports of allergens precipitating emotional symptoms though there were some references to the reverse finding of allergic symptoms from emotions.[1] It would thus seem appropriate to report our observations and attempt to place them into perspective.

The patient was a twenty-five year old married woman who complained of chronic nasal symptoms, frequent bouts of laryngitis and several episodes of hives. An otolaryngologist, noting boggy nasal membranes and slight polypoidal changes with a bluish color of the anterior third of the vocal cords, had referred her for allergy evaluation. To the allergist she indicated that there were marital problems and mood swings, and he requested psychiatric consultation before beginning allergy studies.

The psychiatrist elicited the following history: the patient came from an emotionally turbulent home, mother being emotional and tense and father (incapacitated by "miner's asthma") excitable, wild-tempered and frightening. She was the second of four siblings. She had much resentment against an older brother who was mother's favorite. A younger brother was a "wild drinker" and had several car accidents. Youngest brother had been hospitalized for allergic reactions of some kind. She, too, had been hospitalized several times. She had had a T & A at seven or eight, an appendectomy at thirteen, and a laparotomy two years ago at twenty-three for chronic dysmenorrhea. At that time a diagnosis of endometriosis was made and a uterine suspension and partial oophorectomy had been performed. The dysmenorrhea had continued and become worse despite hormone treatments. She now insisted on having a hysterectomy for the relief of the pain of endometriosis and made thinly veiled suicidal threats saying that when the abdominal pain was especially severe she wanted to drive her car off the road. Sometimes when she experienced pain she wondered if it were her own or someone else's. She said she believed in ESP and various premonitions. These appeared to be connected to a former roommate whom she had had admitted to a mental hospital at nineteen for a "nervous breakdown."

The patient had been married for five years and complained that her sexual life was unsatisfactory. Her husband was partially impotent, little intercourse took place, and when it did it was painful for her. The couple used no contraception because of their religion and the patient feared becoming pregnant. She felt depressed and tense, was self-critical, and had fears of some disaster overtaking her and that no one would believe her or come to help when called. She rejected the possibility of psychiatric treatment and before the year was out she had a hysterectomy.

During the course of the next four years there was only moderate relief from injections of dust and mold extracts; allergy studies were continued. Pertinent to this report were her reactions to hydrocarbons and foods.

She gave a history of physiological and subjective responses to various soluble and volatile materials; this is chemical susceptibility.[2] She reacted to plastics and rubber articles, disinfectants, air fresheners, hair sprays, paints, furniture oils, chlordane,

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fumes from gas stoves and automobiles. These materials would cause nasal discharge and obstruction; she would have substernal pressure and feel that she could not inhale enough air; she would become irritable and feel destructive, sad, tired or withdrawn; this might be accompanied by nausea, headache, and numbness and tingling of the face, chest and limbs. Opening the window would bring prompt relief, but only if the humidity were low.

Hydrocarbon susceptibility was confirmed by the Randolph technique[3] of provocative testing with ethanol. An intracutaneous injection of 0.025 cc. of 1:6250 ethyl alcohol diluted with triple distilled water was given in two sites, making a total dose of 0.05 cc. The results were:

5-9 minutes: Injected arm felt numb. Mild lower sternal pressure and frontal headache. Tingling and numbness around eyebrows, nose and upper lip. Weakness of hands and forearms.

10-11 minutes: Mind felt separated from body. Jittery.

11-13 minutes: Slight cough. Mouth and throat felt dry. Other symptoms receding.

20 minutes: Very talkative and in high spirits.

25 minutes: Felt very tired and like crying. Complained of pain in upper left jaw.

30 minutes: Itching of inner angle of left eye. Nasal discharge.

Provocative food tests were performed according to the method of Rinkel et al.[4] as modified by Hosen[5] and Waickman.[6] The tests consisted of 35 subcutaneous injections of 1:100 glycerosaline extracts* of cereal grains, chocolate, coffee, egg, fruits, herbs, malt, meats, milk, poultry, spices, sugar, tea, vegetables and yeasts. She reacted to more than half of the extracts with physical and emotional discomfort and on several occasions epinephrine injections were given to neutralize the reactions. The test-incriminated foods were then identified for her for the first time and she was able to confirm the test-extract injection results by subjecting herself to a group of food ingestion tests as described by Rinkel.[7]

Her reaction to the subcutaneous injection of milk deserves special mention. After ten minutes she complained of nausea and moderately severe pain in the right paraumbilical area. Spasm of the transverse and ascending colon was palpable; no bowel sounds were heard. An injection of epinephrine promptly neutralized the reaction. She then disclosed that she had been having abdominal distress for some time but had not mentioned it since she thought it might be psychogenic. She went on to relate a history of five prolonged (four to six weeks) episodes, over the preceding fifteen months, of nausea, headaches, fatigue, irritability, brief periods of rapid respirations, constipation, abdominal pain and a hard "sore lump" to the right of her navel. A gastroenterologist had diagnosed colonic spasm and had placed her on a diet of bland foods and milk which she had carefully observed, but without any relief whatsoever.

The other provocative food tests elicited all of the physical and emotional reactions noted earlier with the hydrocarbons. There were also sensations of heat and cold, dizziness, fullness of head and ears, burning sensations within the nose, pains in her eyes and soreness of the lateral cervical area. She had been accustomed to consider these sensations the result of emotional stress only, and their connection with specific foods surprised her. Some of the emotional reactions to the food tests were quite pronounced. On one occasion she experienced acute anxiety and cried out for help. She would sometimes feel depressed and helpless and become tearful. Malaise, drowsiness and marked fatigue would occur although she had started the testing feeling well rested.

Because the emotional reactions appeared to be an important aspect of her positive responses to allergy testing, the same psychiatrist who had seen her five years earlier was invited to participate in a double blind study and record his observations. The patient was cheerful and cooperative. She felt lighthearted, chatted pleasantly, seemed out-going and interested to proceed with the tests. She told him that in the intervening years her father and grandmother had died, one brother was in the Army on combat duty, and that her own marital problems were unchanged. She expressed much positive feeling for the allergist.

The psychiatrist selected the material to be injected. Neither patient nor allergist were aware of the content of the injections which were given by the allergist. The results were as follows:

Subcutaneous injection of 0.1 cc. of Brewer's Yeast

10 minutes: Upper abdominal cramps. Scratchy throat.

13 minutes: Lower right quadrant abdominal pain. Feeling slightly tired.

15 minutes: "Feeling sorry for myself." Nausea. Nervous. Wants to cry. Rapid respiration. Cramps more severe. Arms feel weak.

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* Obtained from Hollister-Stier Laboratories, Yeadon, Penn., and James W. Willoughby, M.D., Kansas City, Mo.

16 minutes: Feels like crying. Jittery. Arms feel weak and tense.
18 minutes: Emotions subsiding. Some substernal pressure.
20 minutes: "Everything wearing off." Normal. Slightly jittery.

The patient volunteered, "Bah! This wasn't one of the spectacular ones. Sometimes I call, 'Dr. M., I need you!"

Subcutaneous injection of 0.1 cc. of normal saline

No reactions were reported or observed.

Subcutaneous injection of 0.1 cc. of milk

4 minutes: Eyes and roof of mouth feel burning.
5 minutes: Pain around bridge of nose. Lips feel full and burning. "Enthusiasm dwindling." Wants to sit quietly without talking.
6 minutes: Frontal headache.
7 minutes: Sharp right paraumbilical pain. Nausea.
8 minutes: Feels difficulty in breathing. Mood subdued.
10 minutes: Pain on left side of face and ear. Wish to lie down and sleep. Cannot think too clearly.
12 minutes: Throat burning. Wants to "snuggle up like a little child on mother's lap."
13 minutes: Wants to be comforted.
14 minutes: "Seem to be snapping out of it." Nausea.
15 minutes: Feeling urinary bladder pressure.

Discussion

It seems clear that the allergens produced physiological changes which were reproducible. But it is not possible to estimate how much the subsequent reactions were a continuing primary response to the allergens and how much to a situation perceived by the patient as being psychologically stressful. What did the allergically-induced nasal obstruction mean to the patient? If it mobilized a fear of smothering and dying, for instance, all the subsequent reactions might be seen as familiar direct manifestations of anxiety or indirect somatic equivalents thereof. Thus, we may not infer a simple or direct relationship between the allergens and the ensuing emotional reactions.

We suggest that the emotional reactions be viewed as the result of the synergistic action of allergic hypersensitivity and psychological predisposition. Fearful and hopeful expectations arising from the past, along with earlier (physical) modes of expressing emotion may contribute generously to current emotional responses. Thus, whatever the immediate stimulus, the emotional responses are often more understandable against the backdrop of past emotional experience than in the light of the current situation alone. This would seem to hold, regardless of the nature of the current stimulus, i.e., whether physical, allergic, psychologic, etc.

We hypothesize that the allergens provoked physiological changes which were perceived by the patient and responded to with a reaction pattern characteristic for her: somatic alarm, anxiety and depression. The communicative content of the emotional response arose out of her personal history of reactions to stress. Its present context included chronic marital discontent, as well as affectionate gratitude and dependency towards her allergist. Her emotional reactions to the allergic changes might be understood as a plea for emotional and physical comfort directed towards him.

What factors contribute to the likelihood of emotional modes of reaction in allergic individuals? Much further observation and critical analysis is needed in this interesting area where allergic and psychological hypersensitivities interact.

Addendum

Since this paper was submitted for publication there have been two very interesting developments in this case. The demonstration of chemical susceptibility by the provocative ethanol test indicated that removal of the gas kitchen range and oven was necessary to eliminate constant exposure to natural gas while indoors. When this was accomplished and the gas inlet to her home was sealed off, she no longer experienced daily restlessness, irritability and "claustrophobia" while in the kitchen; especially when using the range or oven. In addition, she has received hyposensitizing injections of emulsified extracts of several of the foods she reacted to by provocative tests, oral and parenteral. She now tolerates moderate portion of former dietary offenders without physical or mental symptoms.

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Endocrine Effects of Psychotropic Drugs: II. Amenorrhea

Richard I. Shader, M.D., Jeremy P. Nahum, M.D., and Alberto DiMascio, Ph.D.

Menstrual irregularities, particularly amenorrhea, are said to occur as a consequence of psychotropic drugs—especially from high doses of phenothiazines given over substantial time periods. However, long-term placebo-controlled investigations of psychotropic drugs in women of child-bearing age are rare, and it is, therefore, difficult to establish definitively the mechanisms involved and the frequency with which amenorrhea occurs. The issue is further complicated by the common occurrence of menstrual irregularities in women with neuropsychiatric diagnoses. For example, Hanse[1] reported in 1923 that amenorrhea was present in the majority of his female patients (62.5% for catatonia, 50.0% for paranoia and hebephrenia, 60.0% for melancholic, and 45.0% for mania). These figures are clearly in the extreme range and may reflect the additional contribution of factors such as chronicity and diet. In a careful, more recent pre-drug era study of menstrual irregularities in women of child-bearing age, who had been diagnosed as schizophrenic (N=114), depressed (N=81), and elated (N=26), Ripley and Papanicolau[2] found amenorrhea to be present in 18%, 14% and 12%, respectively. Long cycles (35 to 59 days) were reported for 31%, 33% and 19%, respectively. Thus, disregarding diagnostic category, 68 (31%) patients had delayed or prolonged cycles and 34 (15%) reported amenorrhea (a delay beyond 60 days).

Clinical reports dealing with this problem have shown a variety of theories and findings. Polishuk and Kulcsar[3] reported that amenorrhea was found in six out of 11 women treated with chlorpromazine (150-200 mg i.v., for 3-15 weeks), and in all four women treated with higher doses (350-400 mg i.v., for 10 days). The amenorrhea found in the first group was associated with low estrone and normal follicle stimulating hormone (FSH) levels. However, marked increases in FSH were reported for the higher dose group on the tenth day, with return to normal values three weeks after cessation of treatment. This same group[4] studied 200 females treated with oral chlorpromazine. Daily measurements of FSH, LH, and estrone were made which revealed elevated values for all three from the 15-25th days, following which these values returned to normal. One feature of their findings requires comment—three of the six women in the lower dose intravenous route group with amenorrhea also had galactorrhea as did three of the four in the higher dose intravenous route group. The association of galactorrhea with amenorrhea suggests a direct hypothalamic (median eminence) or pituitary effect, as the galactorrhea is thought to be related to decreased median eminence secretion of prolactin inhibitory factor.[5] Other researchers have suggested both pituitary and end-organ inhibition as causes of amenorrhea, as well as possible generalized systemic and toxic actions of these drugs.[6,7]

Whitelaw[8] studied 87 women with problems of infertility and premenstrual distress and found that on low doses of chlorpromazine (50 mg p.o.) nine women with previously regular cycles had delayed menstruation ranging from eight to 16 days. This occurred only when treatment was started 1-3 days prior to expected ovulation, suggesting a critical period for the suppression of ovulation by the drug, a finding consistent with animal research.[9,10] The Whitelaw study[8] employed low doses. Such doses may produce amenorrhea when the drug is started just before ovulation but there is no indication that a continuance of these same levels would produce persistent amenorrhea in subsequent months. Other mechanisms (e.g., increased prolactin) may be involved in the amenorrhea of more prolonged duration which usually occurs later in therapy and at higher dose levels.

Sandison[11] in an early report on thioridazine indicates that amenorrhea was noted by "up to 50%"

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of female patients of child-bearing age. Since details are not given, it is difficult to evaluate this report. The NIMH collaborative study[12] of acute schizophrenia found amenorrhea to be present in 3 to 4% of female patients in all treatment groups (chlorpromazine, fluphenazine, and thioridazine). However, amenorrhea also was reported with the same frequency by the placebo group. Drugs were given only for six weeks in this study, which mitigates against finding amenorrhea in this group of patients. Wallach and coworkers[13] studied all female admissions, between the ages of 16 and 45, to a state hospital over an eight month period and found that 58.6% who were ovulating were on phenothiazines, while 70% of those patients who had amenorrhea were on phenothiazines. They concluded that phenothiazines can be taken by most females without risking persistent anovulation.

Clark[14] found that an experimental phenothiazine (SKF-5354A) produced amenorrhea in six of seven women, and that menses returned three to four months after cessation of the drug in all cases. Also in four female chronic schizophrenic patients with previously regular menses, three developed amenorrhea and the fourth developed metrorrhagia after two months on the drug. Normal menses returned in all four cases after discontinuance of the drug. Urinary gonadotropin secretion was normal in all cases. Cortez and Durazo[15] observed amenorrhea in schizophrenic patients receiving trifluoperazine, chlorpromazine, chlordiazepoxide, and diazepam which was accompanied by low FSH and ovarian hypoactivity. Other clinical and pharmacological studies of the benzodiazepines[16,17] have demonstrated no endocrine effects. Simeon and coworkers[18] reported that two of nine women treated with thiothixene developed galactorrhea and amenorrhea. Imipramine has also been associated with amenorrhea.[19]

Another finding, which compromises any simple formulation of the mechanisms involved in the production of amenorrhea, is that chlorpromazine[20] and other tranquilizers have been found to be effective in the therapy of so-called "functional" amenorrhea.

From the above reports, it can be seen that in psychotic patients amenorrhea has been associated with increased, decreased, and normal urinary gonadotropin levels. In part, this may reflect not only patient-patient differences, but also variability within the same patient at different times, and lack of precision in the methods of measurement, i.e., the bioassay procedures used for urinary gonadotropins. None of these studies utilized any of the newer and more precise radio-immunassay techniques. It is also important to consider the findings of Suwa, *et al*[21] who found 1) stable gonadotropin, estrogen, and pregnanediol excretion patterns in patients whose clinical states were unchanging, 2) decreased gonadol hormones in patients who were in turmoil, and 3) irregular patterns in psychic disturbances of long duration. In view of the inconsistency of the urinary gonadotropin findings and Suwa's demonstration of the linkage between gonadotropin secretion and clinical state, it seems reasonable to concur with Suwa's conclusion that the effects of psychotropic drugs on gonadotropin excretion and possible amenorrhea as a consequence of changes in this, should be of minimal concern in routine clinical practice.

Before any female patient of child-bearing age is placed on a regimen which includes psychotropic drugs, the clinician should take a careful mentsrual history. First of all, this will alert the clinician to evaluate whether the patient is in the early stages of pregnancy.* All psychotropic drugs should be used with caution during pregnancy, particularly during the first trimester. The clinician will also be in a better position to evaluate the amenorrhea should it develop while the patient is under his care. Even then there may be some question, since the anxiety, stress, or psychotic turmoil for which he is treating the patient may in themselves be associated with amenorrhea in non-drug treated patients.

We do not feel that the appearance of amenorrhea should cause alarm. However, it should alert the physician to conduct an adequate medical evaluation to rule out pregnancy and other organic causes. Reduction of dosage is usually a sufficient treatment. In some instances, it may be more reassuring to discontinue the particular drug. It is wise to remember that many patients can be adequately maintained on lower, or even more intermittant,[22] dosage regimens than are required to reduce the distress of the patient who is in the more acute or more florid stage of illness.

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INEVITABLE DEATH AND THE PHYSICIAN

For the physician, who dedicated himself to maintain life, death does not produce anxiety, nor do the limitations of his power to heal. But anxiety is produced by the responsibility coming from a decision he must often take, to halt a fight when he feels it is lost. It is the difficulty to appreciate the moment of his defeat which in fact creates his anxiety. His problem is not to become a persecutor by transforming an inevitable death into martyrdom, after having been a saviour. "Respect for life and the human beings," also means for him respect for death and the dying. Those who are not sick at heart whenever they have to announce to some relative that death is inevitable and nothing more can be done, do not know what it means to be a physician.—Bourguignon, A.: Inevitable Death and the Physician, *Sem Hop Paris Supp,* May 14, 1963.

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THE PRESIDENT'S PAGE

As my term of office draws to a close—for this is my last opportunity to talk to all of you simultaneously—an atmosphere develops not unlike graduating from college. One reflects on why he came to college and what has been accomplished during the four-year span. Then with some trepidation he peers into the future.

A brief comment on a subject which disturbed me led first to a committee, then to a progressive involvement in what is best for patients and for the doctors who take care of them. Actually we were all motivated to study medicine, not to take care of a particular patient, but to provide health care for "people".

The details of what has been accomplished do not belong here. However, the emphasis on communication is bringing us closer together in our united effort to plan for and deliver the best health care possible at a reasonable cost to the bodies, minds and souls of our patients. The art and science of medical practice and planning for its progressive improvement are being benefited by intelligent and repeated collision of the minds. Our thankfulness to God and our forefathers for the heritage of the American way of life is a constant reminder of the responsibility that falls on every individual simultaneously with every privilege. It is a reminded that not complacency but carefully contemplated and courageous action are necessary to preserve the system of free enterprise, necessary to re-direct the accelerating flow of power away from centralized government back to the local community, necessary to introduce conservation into a prodigal economy. The legislators themselves appreciate the effectiveness of COMPAC and AMPAC and of sundry individual efforts.

What lies ahead? Of course the specifics cannot be predicted, but a general course can be charted and the sights set. Here surrounded by illness and tragedy most of us are privileged to be well. Why? And what is each of us doing to deserve this privilege? An increasing number are concerning themselves with community activities beyond their medical contribution: schools, churches, service groups, politics. For some years the image of the physician suffered from a campaign of public disparagement, but the tide has turned and for a reason. The image is not contrived. It is the result of action, not just a design for action. Today's physician is forward-looking in the methods and material used in his practice. He is also alert to other developments which may affect even more the lives of his patients and his own. He is aware that extrinsic controls, advertised to improve medical care, can be made so general that incentive, gratification, and then quality will be diminished. And medicine will only be the first prey to this socialistic octopus.

We must continue to adjust our individual and collective practices as we continually seek to improve the quality of medical care delivered, to be selective in our diagnostic testing and therapeutic measures without being parsimonious, and to be restrained as our charges are adapted to the changing times. We must take an even more active part in the political and social health of our people. If government *of* the people is really to be *for* the people, then it must absolutely be *by* the people. You are highly respected. You are leaders in your community. I believe in you and the people you can lead. The government is yours. Do not let it go.

E. Tremain Bradley, M.D.

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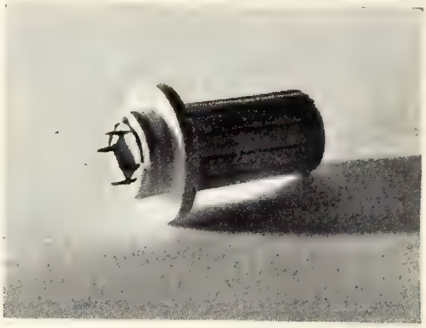

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FROM THE GENERAL MANAGER'S OFFICE

William R. Richards, M.D., *General Manager*
160 St. Ronan Street, New Haven, Conn.
Telephone 865 0587

Peter F. Villano
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

COUNCIL MEETING
Wednesday, March 6, 1968

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin were: Drs. Bradley, Gardner, Grendon, Caplan, Fabro, Hess, Rogol, Cramer, Abbot, Spitz, Hastings, Nolan, Jacobson, Jr., Grant, Johnson, Petrie, Pelz, Wilson and Granoff.

Also present: Mrs. Lindquist, Mr. Villano and Dr. Richards.

Absent were: Drs. Polivy, Brandon, Egan, Shepard, Ayres, Palomba and Roch.

II. ROUTINE BUSINESS

Date of Next Meeting

The next meeting of the Council will be held on Wednesday, March 27, 1968, starting at 1:30 P.M.

III. OLD, NEW AND SPECIAL BUSINESS

Report—Committee on Hospitals

It was VOTED to accept as information a report field by this Committee on the subject of "Hospital Costs and Related Matters".

Being apprised that a Subcommittee of the Senate Finance Committee will begin hearings on the costs of medical care, including hospital costs, in early April and with a view toward preparing a statement on hospital costs for the Society to present at these hearings, it was further VOTED to request the President to appoint a special Ad Hoc Committee to review and supplement the report of the Committee on Hospitals on this subject and to prepare a report (statement) thereon for transmittal to the Senate Sub-committee. The Ad Hoc Committee to be appointed by the President will include Kurt Pelz, Wallingford and Bernard A. Burmham, Waterbury.

Report—Committee on Rural Health

It was VOTED to adopt a resolution, submitted in a report filed by this Committee, as follows:

RESOLVED: That the Connecticut State Medical Society adopt and help to implement, through the component county medical associations, the five-point program listed below:

1. Coordination of efforts or rural communities with adjacent towns or urban centers to analyze existing patterns of response to medical emergencies.
2. Implementation by rural and urban communities of a medical service area program for emergency medical transportation facilities and health personnel.
3. Adoption by rural and urban communities of a model ambulance ordinance spelling out standard of ambulance equipment, personnel and operation, liability insurance requirements, maintenance of records.
4. Provision by rural and urban communities of a program of first aid instruction for the non-medical people most frequently called in rural emergencies, especially police, sheriffs and ambulance crews.
5. Development by rural and urban communities of a continuing campaign of first aid and self-help instruction for rural families, particularly young people through the schools, youth organizations and other educational channels.

Report—Committee on Public Health

A series of reports filed by this committee were acted on as follows:

(a) It was VOTED to approve a recommendation that the Commissioner of Health be requested to appoint an Advisory Committee on the Abused Child, and that, if appointed, the Advisory Committee's membership include one or more members of the CSMS Committee on Public Health.

(b) It was VOTED to approve a recommendation that a State Health Department pamphlet on "Suggested Recommendations for Immunization Against Poliomyelitis" be distributed to all Connecticut physicians by the Health Department.

(c) It was VOTED to approve a recommendation that annual routine toxoid boosters of all kinds be discontinued; that routine boosters in individuals known to have had primary immunizations, including a reinforcing dose, be given only at ten-year intervals; and that emergency boosters be given no closer than one year apart. It was further VOTED to notify the State Commissioner of Health of this action.

(d) Pursuant to the Committee's study of proposed regulations to implement several bills on control of air pollution, enacted by the 1967 General Assembly, it was VOTED to adopt a resolution submitted by the Committee (with minor amendment) as follows:

WHEREAS: The control of air pollution is vital to the public health; and

WHEREAS: The Connecticut State Medical Society has supported the enactment of statutes to control pollution of the air; therefore be it

RESOLVED: That Council of the Connecticut State Medical Society approve proposed regulations that would implement statutes concerning control of air pollution which were enacted by the 1967 General Assembly.

It was further VOTED to notify the Committee on State Legislation of this action.

Report—Public Relations Department

It was VOTED to accept, with thanks and commendation, a report on "Scientific Funding Bureau" prepared by the Public Relations Director, Mr. Villano. In brief, the report lists and describes sources of funding for scientific activities which might be available to the Society from pharmaceutical houses, foundations, etc. It was recommended that the Council's Fiscal Advisory Committee make use of this report when considering proposals for scientific programs received from CSMS Committees, Sections, etc.

Report—Public Relations Division

It was VOTED to accept a report filed by this Division which recommended that the Society make an annual award to a physician for outstanding community service, starting in 1969. A plaque to accompany the award will be furnished by the A. H. Robins Co. The selection of physicians to receive the award will be left entirely to the Society, and a mechanism for soliciting nominees from the component county medical associations is provided by the report. It was further VOTED that, once begun, this award program will be reviewed and evaluated annually.

Reports—Fiscal Advisory Committee

A series of reports of the FAC were acted on as follows:

(a) It was VOTED to approve the recommendation of the FAC that the Society's annual contribution to the Connecticut Committee on Food and Drugs be increased from $75 to $100.

(b) It was VOTED to approve a recommendation of the FAC that, to correct a mathematical error made in drawing up the General Manager's pension program in 1962, an additional annual allocation of $384.89 be authorized with which to implement this purpose.

(c) It was VOTED to approve a recommendation of the FAC that a proposal of the Public Relations Division-Committee on Public Health to plan and conduct a "Physicians' Workshop on Sex Education" be approved, and that the expenditure of up to $1500 be authorized for this purpose. However, it was further VOTED to strongly urge the Division-Committee to seek funds from one or more sources listed in the PR Director's "Scientific Funding Bureau" with which to cover all or part of the costs of holding this Workshop.

Endorsement—Nominee for AMA Board of Trustees

Having been informed that the Massachusetts Medical Society has endorsed Dr. Donald R. Hayes, Springfield, Mass., as a nominee for the AMA Board of Trustees at the June meeting of the AMA House of Delegates, the Council VOTED unanimously to endorse Dr. Hayes' nomination and to inform all delegate members of the AMA House of Delegates of this action. It is understood that AMA Delegates from six New England States will support this nomination and will work actively to assure Dr. Hayes' election to office. The MMS will be notified of this endorsement.

Reports—Committee on Medical Economics and Insurance

On a series of reports filed by this Committee, the following actions were taken:

(a) It was VOTED to approve the recommendation of the Committee that, in a particular instance of complaint, the maximum liability for payment of the underwriter for the Society-sponsored Major Medical Plan be set at an amount stipulated by the Committee, and to inform the member and the Plan's administrator of this action.

(b) It was VOTED to accept a report of the Committee concerning an instance of complaint about certain promotional material being distributed by the administrator of one of the Society-sponsored insurance plans, and to approve the Committee's recommendation that all administrators of Society-sponsored plans be informed that, in the future, any promotional materials which go beyond normally accepted standards for brochures and advertisements must be submitted to the Committee on Medical Economics and Insurance for prior review and approval.

(c) It was VOTED to approve a recommendation of the Committee that the Council grant authorization for Society-sponsorship to a "Group Personal Catastrophe Insurance Program" which will be administered by Group Insurers, Inc., New Haven, Conn.

(d) It was VOTED to approve a recommendation of the Committee that the Council grant authorization for Society-sponsorship to an optional "rider" to the sponsored Disability Income Program, which would offer supplemental benefits to be applied to daily hospital charges in amounts of from $5 to $30 per day. Administrator: The Eade Agency, Hamden, Conn.

(e) It was VOTED to approve a recommendation of the Committee that the Council grant authorization for Society-sponsorship to a "Disability Income Plan, Guaranteed Renewable to Age 70" which would offer a number of flexible variations of the present Disability Income Program, some to the advantage of the older members and some to the advantage of younger members. Administrator: The Eade Agency, Hamden, Conn.

Communication—HCMA Board of Directors

Pursuant to legislation enacted by the 1967 General Assembly, which authorizes judges to determine the limit of fees charged by physicians for medical testimony given in courts, the Council was apprised that the Hartford County Medical Association had surveyed its membership as to "usual and customary charges" for such testimony and was desirous of informing pertinent judges presiding in pertinent courts in the Hartford County area of the medical witness fees that should be considered reasonable in that area. It was VOTED to authorize the Board of Directors to implement this proposal, provided it was made crystal clear to the judiciary concerned that such fee levels were applicable to the Hartford County area *only*. It is understood that the Society's Conference Committee with the State Bar Association is planning to review the over-all intent and effect of this legislation, and report on the subject to their respective parent bodies.

Communication—The Naugatuck Valley Medical Society

It was VOTED to accept as information, and with thanks, notice from the NVMS that its membership had voted unanimously to express confidence in the mechanisms for individual representation offered to members at all levels of organized medicine, and in their elected representatives in the New Haven County Medical Association, the Connecticut State Medical Society and the American Medical Association. The NVMS action was prompted by the resolution adopted by the CSMS House of Delegates, December, 1967, which replied to the "challenge" to organized medicine issued by the Medical Committee for Human Rights.

Report—Ad Hoc Committee on Feasibility of CSFS Study of Medical Care

A report of this Ad Hoc Committee, submitted by Orvan W. Hess, Chairman, was acted on as follows:

(a) It was VOTED to accept the Ad Hoc Committee's opinion that it is *not* feasible for the Society to undertake such a study as an independent project.

(b) It was VOTED to accept the Ad Hoc Committee's recommendation that the Society seek to participate actively in similar studies now being planned by the Connecticut Regional Medical Program (in conjunction with the AMA) and to request the President, E. Tremain Bradley, as a "committee of one", to discuss with the Planning Director of CRMP, Henry T. Clark, Jr., the mechanisms through which the Society's participation could be most effective. Dr. Bradley is to report to the Council on the conclusions reached at this discussion with Dr. Clark.

(c) It was VOTED to dissolve the Ad Hoc Committee, with thanks, and to provide for the appointment of a new permanent committee to participate actively in the CRMP projects (pending Dr. Bradley's report as called for under (b)).

Further Presentation and Discussion of Connecticut Regional Medical Program

Henry T. Clark, Jr., New Haven, Planning Director, and three other members of the CRMP staff joined the Council for approximately two hours of review and discussion of some of the major projects that CRMP has under study, in the final planning stages, or ready for implementation (using HEW operational grants). The presentations covered a number of "thrusts" which CRMP intends to make in various areas of health and medical care in keeping with its "guiding philosophy". On behalf of the Council, the Chairman thanked Dr. Clark and his associates for coming to the meeting and furnishing this information. A number of Council members expressed the opinion that they were unable to understand the value to better patient care of much of what was presented, and that a good deal of it sounded rather ominous with respect to continuation of the private practice of medicine. Beyond that, no formal action was taken in this matter.

Report—Committee on Third Party Payments

It was VOTED to approve a recommendation of the Committee, concerning the proposed CMS "Century Contract" as follows:

That the Council apprise the State Insurance Commissioner, in writing, of the CSMS evaluation of the propsed CMS Century Contract, stressing at least three important factors as follows:

1. That the proposed Contract is inflationary (in many of its allowable "maximum" payments, within different types of practice and with respect to levels of usual and customary charges throughout the state).
2. That the propoed "new" contract (in concept) is contrary to national trends and developments among third party payors (i.e., it offers a uniform state-wide payment schedule instead of the flexible usual and customary charge method.
3. That the proposed Contract (not using the usual and customary charge method) fails to allow for servicing of Blue Shield programs on a national scale for industrial purchasers having (branch plant) group members in several states.

N.B.: The foreging is a summary of the proceedings and actions of the Council on March 6, 1968. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.

Placement Wanted

ALLERGIST—Board eligible internist with special interest in allergy wishes to locate in Connecticut. Connecticut license, presently completing military duty. Wishes to practice with a partner or in a group. Available about March 10, 1968.

OBS-GYN—Board certified Ob-Gyn Fellow, age 32, University trained, military service recently completed. Seeks group or association practice.

NEUROLOGIST—Board eligible, seeks clinical affiliation in Connecticut. Considerable experience in Internal Medicine, Neuropathology and Psychiatry. Connecticut license, military obligations satisfied.

RADIOLOGIST—40 year old, Chief, university radiotherapy department. N.Y., Conn. licensed. Intersted in private practice of radiotherapy in downstate N.Y. or western Connecticut areas.

Placement Opportunities

HOUSE PHYSICIAN—Diversified duties in voluntary, accredited hospital. Connecticut license required. 45 hours a week, Monday through Friday; no weekends. Immediate placement. Excellent salary. Write: P.O. Box 3474, Bridgeport, Connecticut 06604.

NEWLY APPROVED 3 YR. RESIDENCY now offered at Hartford Hospital with combined clinical experience at Newington Hospital for Crippled Children and The Gaylord Hospital. Teaching affiliation with Yale-New Haven Medical Center. Supervision under full-time psychiatrists. Experience available in a variety of child and adult disorders. Write: Carl V. Granger, M.D., Hartford Hospital, CCUl, 80 Seymour Street, Hartford, Connecticut 06115.

WANTED—Internist, Board eligible, to associate with two busy young internists in modern spacious offices in a New Haven suburb. Excellent hospital facilities available. A fine opportunity for rapid growth. For further information, contact: Marvin P. Zimmerman, M.D., or Edward S. Scherr, M.D., 960 Main Street, Branford, Connecticut 06405.

NEW YORK State Narcotic Addiction Control Commission has full or part-time openings to provide psychiatric services for resident addicts in rehabilitation centers in the Mid-Hudson River Valley area (Woodbourne, Beacon, Stormville, New York). Exceptional opportunity to supplement private practice in areas with minimal psychiatric coverage, or to begin long-range association with dynamic, challenging, total approach rehabilitation program. Ed. Cert or Elgbl. Write Assistant Commissioner—S. Seymour Joseph, M.D.—Dept. P-24, 1855 Broadway, New York, New York 10023.

PSYCHIATRIC RESIDENCIES—available in a community oriented mental hospital. Comprehensive treatment facility for central Conn. area. Associated with Yale University Departments of Psychiatry and Neurology which provides supervision and opportunities for training in areas of special interest. All Senior Administrators and Training Director Board certified and on faculty of Yale. Special arrangements can be made for residents to be accepted for degrees in community mental health and hospital administration at the Yale School of Epidemiology and Public Health. Visiting lecturers. Seminars in transcultural psychiatry. Personal analysis can be easily arranged. Stipends: First year $9050; Second year $9530; Third year, $10,380. Many fringe benefits. Please send all particulars with first letter to Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

ASST. DIRECTOR OF PSYCHIATRIC TRAINING—Board certified, will consider a Board eligible candidate to assist in directing a three-year approved psychiatric residency program at 1600-bed, community-oriented, geographically decentralized mental hospital. Also assist in coordinating psychiatric education for nurses, psychologists, social workers and occupational therapists in approved university affiliated programs. Previous teaching experience desirable. Qualified candidates may be considered for other senior staff positions with starting salary up to $23,430. Active, well-established program, with emphasis on psychodynamic and community psychiatry. Affiliated with Yale University, Wesleyan University, UConn, Connecticut College for Women, Hartford Hospital, Alcoholism and Drug Dependency Treatment Centers, Children's Services and four community clinics. Starting salary: $18,680 to $23,060, depending on training and experience. Excellent fringe benefits. All particulars should be sent in first letter. Annual leave to attend medical conventions. Write: Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

PSYCHIATRIST—Community-oriented mental hospital. To work in or direct a 500-bed comprehensive mental health center, one of several units in a geographically decentralized 1600-bed hospital. Opportunity for teaching, clinical work, and research. To with or direct a team of social workers, psychiatric residents, psychologists, occupational therapists and approximately 190 nursing staff personnel. O.P.D., day care, in-patient consultation and emergency care available. Qualified candidates may be considered for other senior staff positions with starting salaries up to $23,430. Starting salary $16,970 to $22,340, depending on training and experience. Liberal fringe benefits. All particulars should be sent in first letter, including references, to: Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

GENERAL PRACTITIONERS (Internist or G.P.)—Growing residential community of 12,000 in greater Bridgeport area has recently lost two family physicians and is desirous of obtaining at least two replacements. Hospitals nearby and staff appointments favorable. Fully equipped offices readily available for lease or purchase.

WANTED—Young pediatrician to join two internists and two general practitioners in a new medical building complete with laboratory and radiology services in a beautiful suburb of Hartford, Connecticut, Type of arrangement offered flexible.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

SAVE THE DATE

WEDNESDAY, JUNE 5
10:00 A.M. to 4:30 P.M.

Park Plaza Hotel, New Haven

Second Physicians Workshop on Sex Education

Invitations Coming

The Ethics Of Contractual Arrangements Between Physicians And Clinical Laboratories

This subject appears to be causing some degree of confusion among individual practitioners and their medical organizations. For this reason, the following Council-approved report is published for the information of the membership. The report was prepared by the Committee on Preliminary Study of Censorship Questions.

The Committee was requested to consider the ethics of contractual arrangements between physicians and clinical laboratories, especially as to the fees charged to patients by physicians for laboratory tests done by such laboratories.

Question: If a physician contracts to pay a laboratory a fee, monthly or otherwise, to perform tests, singly or in unlimited amount, is it ethical for the physician to charge the patient a fee which would in effect result in a profit to the physician for a service not performed by him?

The Committee on Preliminary Study of Censorship Questions considers any arrangement with a clinical or medical laboratory whereby the physician receives profit from such an arrangement with the laboratory for its services by his merely acting as a middle man is not within the tradition and ethics of the medical profession.

A physician is free to make any arrangements with laboratories which will benefit his patients, provided that he shall have assured himself of the reliability and quality of such laboratories and their work. Any financial benefits from such arrangements shall be passed on to the patient without his making a profit (as in the wholesaler-retailer arrangement in business). He may bill the patient separately for the laboratory fee, or make a charge to cover the cost of the laboratory fee, but it shall be unethical for any physician in Connecticut to make any financial arrangement with a clinical laboratory wherein he makes a profit, as in a business, for services not performed by himself.

BASIS FOR OPINION

(a) *Section 7 of the AMA Principles of Medical Ethics:*

"In the practice of medicine, a physician shall limit the source of his professional income to medical services rendered by him, or under his supervision, to his patients."

(b) *Billing Procedure for Laboratory Services:*

1. The practice of pathology is an integral part of the practice of medicine.
2. All physicians should bill their patients directly, and
3. In exceptional cases, when it is not possible for the laboratory bill to be sent directly to the patient, the referring physician's bill to the patient should indicate the charges for laboratory services, including the name of the physician director of the laboratory, as well as the charges for his own professional services. (AMA Judicial Council, 1965)

(c) *Cooperative Diagnostic Laboratories:*

Concerns known as "cooperative diagnostic laboratories" have been organized in which practicing physicians participate as "members". Information indicates that organization is effected in such a manner that control will lie in the hands of the promoters and directors of these schemes and that practicing physicians are then expected to refer work to the laboratories operated by the concern. As a consideration for such referrals, the physician members receive from the laboratories compensation varying with the amount of work referred. The Judicial Council is of the opinion that schemes of this kind are unethical and directly opposed to the interest of scientific medicine. (AMA House of Delegates, 1930)

Approved by the Council, 11/16/67

WOMAN'S AUXILIARY

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Reminder—The annual meeting of the Woman's Auxiliary to the Connecticut State Medical Society is May 1 at the Town and Country Club, Hartford. A petite luncheon will be served at 1 P.M. The program will include Mrs. Thomas Anton, Director of the Woman's Auxiliary to the A.M.A. Mrs. Anton is a past president of the Woman's Auxiliary to the Maine State Medical Society. We hope to see many of our members to honor her and our outgoing president, Mrs. Anthony Cipriano.

1968 Convention

St. Francis Hotel, San Francisco, Calif.

June 16 to 20

Conducted tours through a unique rehabilitation mobile unit and an afternoon of continuous health education films will be new features at the 45th Annual Convention of the Woman's Auxiliary to the American Medical Association. Headquarters for the June 16-20 meeting will be the St. Francis Hotel, San Francisco, Calif.

Highlighting the four-day session will be the new mobile demonstration unit called "Homemaking Unlimited." This five-ton coach, sponsored by the School of Home Economics of the University of Nebraska, shows handicapped housewives how they can be self-reliant homemakers despite physical limitations. During the convention the unit will be displayed on Powell St., across from the St. Francis Hotel.

On Sunday, June 16, the Auxiliary will hold a reception for the president, Mrs. Karl F. Ritter, Lima, Ohio, and president-elect, Mrs. C. C. Long, Ozark, Ark., from 5 to 7 p.m.

The convention will formally open at 9 a.m., Monday, June 17. Mr. Philip Lesly, president of The Philip Lesly Co., a Chicago-based public relations firm, and counsel on PR and communications to the AMA, will deliver the keynote address.

Monday luncheon will honor the leaders of women's volunteer organizations throughout the United States. Featured speaker will be Henrik L. Blum, M.D., Clinical Professor of Community Health Planning, University of California School of Public Health. Dr. Blum will discuss "Program Planning and Implementation."

Milford O. Rouse, M.D., AMA President, will be the guest speaker at the Tuesday, June 18, luncheon honoring national Auxiliary past presidents and AMA Officers, Trustees and wives. At this time Mrs. Ritter will present the Auxiliary's contribution to the American Medical Association Education and Research Foundation. Last year's gift totaled $384,649.

The Tuesday afternoon meeting will feature a program by the Communications Committee relating to state publications. Following this program, films, including several on sex education, drug abuse, physical fitness and nutrition, will be shown for the remainder of the afternoon. This new feature will provide Auxiliary members with a catalog of available health education materials to be used in conjunction with existing Auxiliary programs.

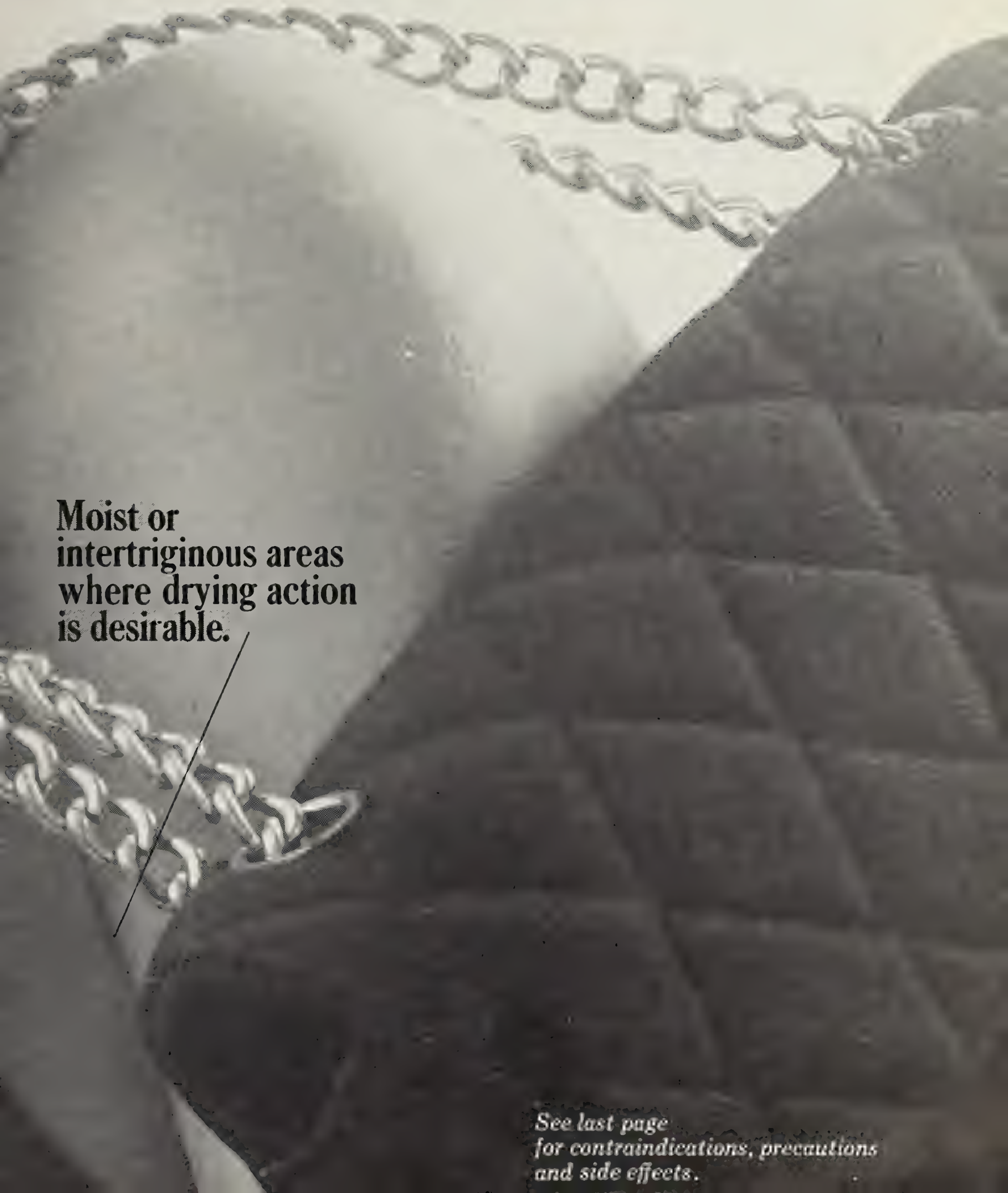
The postconvention conference, usually scheduled for Thursday morning, will be held on Wednesday afternoon to give Auxiliary members free time on Thursday to visit areas of San Francisco. The Board of Directors will meet Thursday morning, instead of Wednesday afternoon.

The Auxiliary will also sponsor a program of daily activities for the pre-teens and teenagers of Auxiliary members and guests. Lunch in Chinatown and a cable car ride are among the events being considered.

Local arrangements for the convention are under the direction of Mrs. Lloyd Gillin and Mrs. Don C. Musser, both of San Francisco. Mrs. Ralph B. Eusden of Long Beach, Past President of the Auxiliary, is honorary chairman.

Hairy sites where creams and ointments do not spread or penetrate readily.
Exposed areas where cosmetic considerations are important.

An invisible topical for many dermatologic problems



Moist or intertriginous areas where drying action is desirable.

See last page for contraindications, precautions and side effects.

Structurally unique topical steroid in propylene glycol vehicle produces rapid response in many dermatoses.

Synalar Solution produces rapid antiinflammatory, antipruritic action through its unique topical corticosteroid, fluocinolone acetonide. The propylene glycol vehicle provides additional benefits for therapy at problem sites where it is difficult to achieve contact between the lesion and medication—or where creams or ointments may make the lesions worse. Synalar Solution has proved particularly valuable in the symptomatic treatment of seborrheic dermatitis of the scalp, nasolabial folds, eyebrows, ears, and in flexural folds such as the axillae, inframammary, umbilical and anocrural areas. It has also been reported to achieve excellent results in the adjunctive management of atopic dermatitis, contact dermatitis, neurodermatitis, nummular eczema, psoriasis, and sweat retention syndromes in these problem sites.

Penetrates the hairy sites.

In many areas of the body, hair gets in the way of treating the underlying dermatitis. The propylene glycol vehicle of Synalar Solution permits penetration and dispersion at sites where creams and ointments do not readily penetrate. May be applied without matting of hair.

Ideal for moist or intertriginous areas.

Propylene glycol is strongly hygroscopic and is especially useful where sweat retention is a problem. Its low surface tension permits easy spreadability in difficult-to-treat body areas. A number of studies have also shown that propylene glycol has inherent antimicrobial activity.

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Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components.

Precautions: In some patients with dry lesions, the solution may increase dryness, scaling, or itching. Application to denuded or fissured areas, such as genital or perianal sites, may produce a burning or stinging sensation. If this persists and dermatitis does not improve, discontinue medication. Although propylene glycol has antiseptic activity, there should be careful initial evaluation and follow-up of infected sites. Incomplete response or exacerbation of lesions may be due to true infection, which requires susceptibility testing and appropriate therapy. On the other hand, saprophytic or low grade infections may clear spontaneously under the influence of Synalar Solution alone. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Side Effects: Side effects are not encountered ordinarily with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions.

Availability: Synalar (fluocinolone acetonide) Solution 0.01% in a propylene glycol vehicle with citric acid as preservative. 20 and 60 cc. plastic squeeze bottles. *Also available:* Synalar (fluocinolone acetonide) Cream 0.025% – 5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01% – 15, 45 and 60 Gm. tubes and 120 Gm. jars. Ointment 0.025% – 15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream – 5, 15 and 60 Gm. tubes.

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SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

Synalar®
(fluocinolone acetonide)
Solution
0.01%

An invisible topical

In Memoriam

Cerrone, Luke J. — New Haven; Bologna University School of Medicine, 1938. Dr. Cerrone was a practicing physician in the New Haven area for nearly 30 years. During World War II he served in the Army as a Major. Dr. Cerrone was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was a member of the Board of Directors of St. Raphael's Hospital. Dr. Cerrone died March 3, at the age of 60.

Donnelly, Stephen P. — New Britain; Georgetown University Medical School, 1924. An orthopedic surgeon, Dr. Donnelly practiced in the New Britain area for 41 years. He was a member of the New Britain Medical Association, the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American College of Surgeons. Dr. Donnelly died February 17, at the age of 73.

Huleatt, Thomas R. — Hartford; Columbia University School of Medicine, 1949. Dr. Huleatt was a practicing pediatrician in Hartford for over 14 years. He was a clinical assistant at Hartford Hospital and Assistant Pediatrician at the Newington Hospital for Crippled Children. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Associaion. He was a Fellow of the American Academy of Pediatrics. Dr. Huleatt died December 21, at the age of 44.

Lynch, Edward J. — Shelton; University of Pennsylvania School of Medicine, 1908. As Superintendent of Laurel Heights Hospital in Shelton, Dr. Lynch devoted his medical career to transforming the institution into a modern hospital widely recognized in the field of tuberculosis and pulmonary disease treatment. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American Thoracic Society, the American College of Physicians, and the American College of Chest Physicians. Dr. Lynch died February 18, at the age of 83.

Wiggans, R. Glen — Norwalk; Cornell University Medical School, 1946. Dr. Wiggans was a urologist in Norwalk for 13 years. He was associated with Norwalk Hospital. Dr. Wiggans served in the U.S. Air Force as a captain and flight surgeon. He was on the teaching staff at Bellevue Hospital and Cornell University Medical School. Dr. Wiggans was past president and treasurer of the Norwalk Medical Society. He was a member of the Norwalk Medical Society, the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Urological Association. Dr. Wiggans died February 23, at the age of 45.

BOOK REVIEWS

PROGNOSIS: A GUIDE TO THE STUDY AND PRACTICE OF CLINICAL MEDICINE. Edited by Leslie A. Osborn, M.D. Charles C. Thomas, Publisher, Springfield, Illinois, 1966. 286 pp. $10.00.

Reviewed by: LOUIS H. NAHUM

The purpose of this book is to prepare medical students for their clinical work with patients, to present systematically the sequence of clinical procedures and the reasoning processes by which patient's problems are worked out and rational therapy planned. The thesis of the author is that prognosis is the key to treatment and especially to the working relationship between doctor and patient.

What the student will get out of these rich pages is how to develop one's personal influence, how to deal with patients as people, how to deal with children, how to understand families, how to develop team work with colleagues and with community relationships. The author clarifies the relationship of patient care to education to research and to administration keeping always in focus practical objectives of prevention and treatment. But there is much more, for the book offers suggestions about learning, utilizing one's time, use and misuse of memory, how basic science and clinical medicine are, each complimentary to the other. Then there is sound advice on how to study.

This marvelous little book is from the pen of a physician rich with thirty-six years of experience. It contains much about the personal and inter-personal aspects of medical practice, and how one may learn to develop medical practice on a strong personal foundation. These are results of experience and research concerning education and its application to medicine. With rapid expansion of knowledge and rapid obsolescence of older knowledge, the author makes some wise suggestions about how to adhere to a pattern of life-time learning, how to remain a student for life.

The book is a treasure of wisdom and experience full of aphorisms and wise examples of his purposes. It may emphasize its aim to reach the medical student, but every physician will be wiser and more secure the more he makes the philosophy of this book an integral part of his continuing activity. Shining through its pages is the wise physician who has learned much and successfully conveyed his wisdom to his readers.

MONGOLISM. Ciba Foundation Study Group No. 25. Edited by G. E. W. Wolstenholme and Ruth Porter. Little, Brown and Company, 1967. 99 pp. with 23 illustrations.

Reviewed by: JOHN L. MEYER, II

The Ciba Foundation publishes the proceedings of conferences held under its auspices, and the volume MONGOLISM is one of the cardboard-bound booklets recording one-day symposia, the one in question having been held in May, 1966. The participants, headed by Lord Brain (a trustee and chairman of the Executive Council of the Foundation), includes scientists from the world over.

The papers and discussions are exploratory, involving statistical and parametrical approaches to this particular area of chromosomal abberations.

Lord Brain's introduction is a brief but enchanting account of the life and work of John Langdon Haydon Down, who, in 1866, wrote the classical description of the child known as a mongoloid, mongol or victim of Down's syndrome. In typical British preoccupation with lineage, Brain —who is the grandson-in-law of John Down—finds family connections between that worthy and Charles Darwin and Maynard Keynes, among others.

Much of the material covered in this book would be of interest essentially to those who have gone deeply into the subject of Down's syndrome, and are oriented to the problems of the ultimate cause of chromosomal variations, illumination of kynetics in the study of mosaic mongoloids, and problems of DNA synthesis and replication. The discussions and exchange of ideas following each presentation are for the most part—but not always—abstruse.

The general discussion that concludes the conference offers some interesting observations by the participants and reveals them as human beings.

The general reader will not find much in the heart of the scientific presentations to orient him to mongolism as a whole, for such orientation is assumed. The brief time necessary to peruse this slim booklet (under 100 pages) could prove well spent, however, if the reader enjoys contemplating the advancing concepts of science and the effects of general social enlightenment. The idea the mongolism represents an ethnic regression is no longer tenable, either scientifically or sociologically, and remarks on this subject and on the very use of the term mongolism should prove illuminating for any reader.

THE PHYSIOLOGICAL CLOCK. Revised second edition. Edited by Professor Erwin Bünning. The Heidelberg Science Library, Volume 1. Springer-Verlag New York Inc., 1967. 167 pp. with 126 figures. $3.00.

Reviewed by: LOUIS H. NAHUM

This monograph is limited to considerations of the biological measurement of time in which unicellular organisms as well as cells of higher plants, animals and man utilize periods of approximately twenty-four hours. The author addresses himself to the present state of our knowledge of the physiological nature of this clock and the manifold means by which the organism uses this clock. Graciously he "hopes to attract new workers into this fascinating field, workers who will contribute through their discoveries to a speedy outdating of this presentation."

Many of the fourteen chapters are introduced by scholarly quotations and each chapter is followed by an extensive bibliography. This book is not for the practicing physician, but he should know that fascinating knowledge exists in biological clocks which may one day assume important clinical implications.

Rights Of Patients In Research

What are the rights of patients who claim damages from clinical investigations by medical researchers?

U.S. courts have not yet considered such cases, but the general rule of "informed consent" probably applies, the director of the American Medical Association's law division told the First World Meeting on Medical Law recently in Ghent, Belgium.

Under this rule, physicians have a duty to obtain consent from a person who has the authority to give it before performing treatment that legally might be considered assaut.

This rule probably would be strictly applied for adults who participate in experiments without the expectation of medical benefit, said Bernard D Hirsh, L.L.B.

It would be of questionable legality, however, to use children or mentally incompetent persons in such experiments, even if the parent or guardian consented, he said.

"The answer to the question of how much information a physician must furnish to a patient to avoid legal liability is somewhat complex because it arises out of two separate and distinct legal obligations," Hirsh said.

One is the necessity to obtain valid consent; the other is that the physician should act with the highest degree of good faith to protect the interest of the patient.

"Thus it appears that the clinical investigator must always provide an investigative subject with an adequate explanation and information regarding the risks . . . that may occur," Hirsh said.

Unless they are to receive needed medical treatment, persons lacking the "capacity to consent," such as children and the mentally incompetent, should not be used for clinical investigation, merely because they are available, he said.

Hirsh pointed out, however, that it may be necessary to use these patients in some instances.

"Some kinds of clinical investigation of children's diseases cannot be accomplished without using children as subjects. Similarly, research on mental retardation might be impossible without the participation of mentally retarded subjects."

"It seems unlikely that public policy would entirely foreclose clinical investigation in these fields . . ." Hirsh said.

AROUND THE STATE

Around The State
Planning Child Welfare Services

A Directory of Child Welfare Services throughout the State is now available for the first time. It is one of the results of a survey of Child welfare services and needs just completed by University Research Institute of Connecticut (URIC). The receipt of the final report of this survey was announced recently by the Connecticut Research Commission, which had made a grant to finance the project.

The team of investigators consisted of: Professor Jean E. Markham, Coordinator of Social Welfare Concentration, Southern Connecticut State College; Dr. Sally Provence, Director of Child Development Unit, Yale University; Dr. Albert J. Solnit, Director of Child Study Center, Yale University; and Professor Edward G. Stockwell, Professor of Rural Sociology, University of Connecticut. Mr. Norman H. Spear, Executive Director of URIC, coordinated the survey.

The made a survey of all identifiable child welfare service organizations in Connecticut and a demographic analysis of Connecticut population through 1975. The information thus gained was the starting point for the development of a comprehensive plan for meeting the future child welfare needs in the state. It was concluded that a fixed plan would soon be outmoded. Therefore the plan presented in the final report includes a research element whereby the changing needs will be monitored continuously to make it possible to incorporate new services into a comprehensive service network for the State.

In putting this far-reaching plan into effect, it is expected that the State Department of Welfare will seek the cooperation of the U.S. Department of Health, Education and Welfare.

Strong Voice Needed

"We are living in a social, economic and governmental climate in which medicine needs the strongest possible voice in order to state the profession's side of the literally hundreds of issues that are being raised for consideration by the public and by the legislative bodies of our nation."

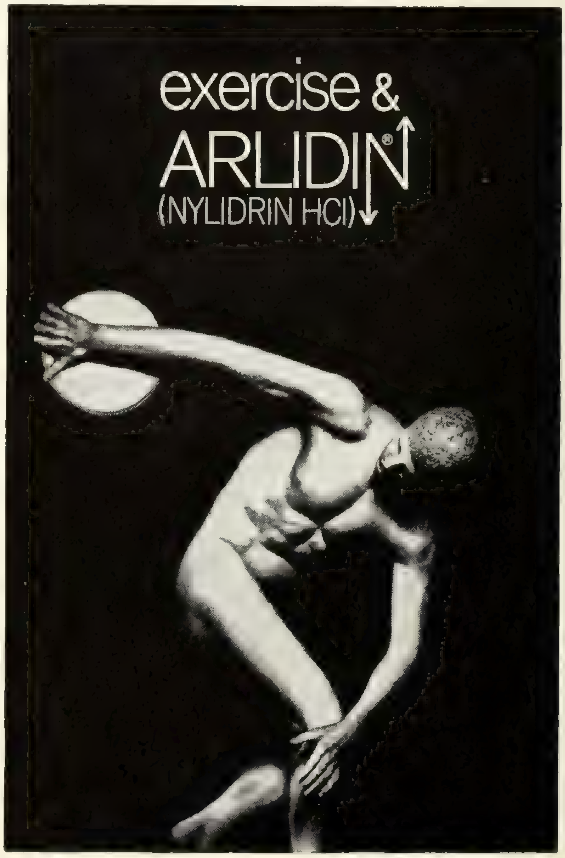
—Milford O. Rouse, M.D.
AMA President

Medicine And Religion

The Connecticut State Medical Society's Committee on Medicine and Religion is presenting a panel discussion entitled "The Doctors' Dilemma in the World of Changing Morals". This program will take place on April 30 at the Hartford Hilton Hotel at 8:00 p.m. This will be the first program at the time of State Annual Meeting being presented on the topic of Medicine and Religion.

Under the capable chairmanship of Francis W. Helfrick, M.D., the Committee is in the process of assembling a panel of four to discuss Abortion and Contraception. The moderator of the panel will be Reverend Dr. Paul B. McCleave, Director of the Department of Medicine and Religion at the A.M.A. in Chicago.

The two physicians on the panel are John Rock, M.D., Director, Rock Reproductive Clinic, Inc., and clinical professor of Gynecology, emeritus, Harvard Medical School; and Abraham Franzblau, M.D., Ph.D. psychiatrist in New York City. Reverend Seward Hiltner, Ph.D., Professor of Theology and Personality at Princeton Theological Seminary and Rev. John J. Lynch, S.J., Professor of Moral and Pastoral Theology, Weston College, Weston, Massachusetts, will be the clergymen on the panel.



MEETINGS

CANCER

May 8 1:30-4:30 p.m.

Current Concepts in Management or Oral Cancer

Peters-Darrow Conference Room

Yale-New Haven Medical Center

Advance registration necessary; fee $5.00

Contact: Office of Postgraduate Education, Yale University School of Medicine, 333 Cedar Street, New Haven, Conn. Phone: 562-1161 Ext. 864

May 16 All Day

Quality of Survival of the Cancer Patient

Hotel America, Hartford

Sponsors: Connecticut Division, American Cancer Society; American College of Surgeons; Vocational Rehabilitation Branch, U.S. Department of Health, Education and Welfare

Description: Discussion of the problems of rehabilitation of the colostomy, mastectomy, and laryngectomy patient; discussion of the cosmetic defects resulting from head and neck surgery. Speakers, Milton Edgerton, M.D., Johns Hopkins; Richard Jessie, M.D. Anderson Hospital; Maus Stearns, M.D., Memorial Hospital of Cancer & Allied Disease; R. B. Turnbull, M.D., Cleveland Clinic Foundation. Registration at 9:00 a.m., medical sessions, 9:30-11:30 a.m. and 1:00-5:00 p.m.; dinner meeting at 7:30 p.m.

Registration (free of charge) limited by invitation to members of selected medical groups.

Contact: Paul G. Kuehn, M.D., 85 Jefferson Street, Hartford; Phone 524-5939

May 22 1:30-4:30 p.m.

Current Concepts in Management of Laryngeal Cancer

Peters-Darrow Conference Room

Yale-New Haven Medical Center

Advance registration necessary; fee $5.00.

Contact: Office of Postgraduate Education, Yale University School of Medicine, 333 Cedar Street, New Haven, Conn. Phone: 562-1161 Ext. 864

MEDICINE

March 27 9:30 a.m.-4:30 p.m.

Symposium on Thyroid Function Tests and Diseases

Manchester Memorial Hospital

Speakers: Herbert Selenkow, M.D., Assistant Professor of Medicine, Harvard Medical School; David Becker, M.D., Associate Professor of Medicine and Radiology, Cornell University Medical College; John Brooks, M.D., Assistant Clinical Professor of Surgery, Harvard Medical School; Bruce Bower, M.D., Clinical Endocrinologist, Hartford Hospital.

Open to all physicians Registration fee $2.00 including lunch

Contact: Martin Duke, M.D., Director of Medical Education, Manchester Memorial Hospital

April 10 9:00 a.m.-5:00 p.m.

Fourth Symposium of the Kidney Foundation of Connecticut

West Haven Veterans Hospital

Description: current concepts of the pathogenesis chronic pyelonephritis; clinical experience with the Giordano-Giovanette diet; recent findings in the immuno-pathology of acute and chronic renal disease; clinical management of the acidonic patient; clinical experience with the use of immuno-suppressive agents in the therapy of glomerculonephritis; clinical management of salt and water balance in chronic renal disease.

Registration Fee: $10.00, including a buffet luncheon

Program Co-ordinator: John Goffinet, M.D., Director of Hemodialysis, West Haven Veterans Hospital

Contact: Thomas Freeman, 357 Whitney Avenue, New Haven; Phone 777-1292

April 18 11:00 a.m.

Newer Aspects in the Diagnosis of Primary Aldosteronism

State Veterans Home and Hospital, Rocky Hill

Speaker: Bruce Bower, M.D., Hartford Hospital

Open to all physicians

Contact: Richard P. Johnson, M.D., Chief of Medicine, State Veterans Home and Hospital, Rocky Hill

April 24 9:30-4:30 p.m.

Connecticut Conference on Prevention of Cardiovascular Disease

Stratford Motor Inn, Exit 53 Merritt Parkway

Sponsors: Connecticut Heart Association, Connecticut State Department of Health, Connecticut State Medical Society

Contact: Mrs. V. G. Schroeder Burham, Chairman 103 Shusted Lane, Greenwich

April 30 11:00 a.m.

Kidney Transplantation

State Veterans Home and Hospital, Rocky Hill

Speaker: Mark W. Izard, M.D., Hartford Hospital

Open to all physicians

Contact: Richard P. Johnson, M.D., Chief of Medicine, State Veterans Home and Hospital, Rocky Hill

May 2-4

Fifth Annual Meeting of the American College of Clinical Pharmacology and Chemotherapy

Claridge Hotel, Atlantic City, New Jersey

No registration fee

May 9 10:00 a.m.

Tuberculosis Control and Eradication in Connecticut

Holiday Inn, Meriden

Sponsored by the Connecticut Thoracic Society and the Connecticut Tuberculosis and Health Association

Open to all physicians; no registration fee

Contact: Nicholas D. D'Esopo, M.D., West Haven Veterans Hospital; Phone 932-2561

May 15 All Day

Heart Diseases in Infants and Children

Yale-New Haven Medical Center

PSYCHIATRY

April 10 1:30 p.m.

Personality Development and Psychopathology

Kettle Building, Norwich Hospital

Sponsor: Connecticut Postgraduate Seminar

Speaker: Maurice E. Linden, M.D., Director, Division of Mental Health, Community Health Services

Open to all physicians

Contact: Vincenzo Cocilovo, M.D., Assistant Superintendent, Norwich Hospital

April 24 12 Noon

History of Psychiatry

Kettle Building, Norwich Hospital

Sponsor: Connecticut Postgraduate Seminar

Speaker: George More, M.D., Medical Director, The Astor Home for Children, Rhinebeck, New York

Open to all physicians

Contact: Vincenzo Cocilovo, M.D., Assistant Superintendent, Norwich Hospital

April 27

Aseptic Meningitis

Speaker: Martha Lepow, M.D., Associate Professor of Pediatrics, University of Connecticut School of Medicine

PEDIATRICS

Cardiovascular Surgery

May 15 9:30 a.m.-4:30 p.m.

Mary S. Harkness Auditorium

Yale University School of Medicine

Description: The postgraduate program is designed to provide the practicing physician with information on emergency problems in the fields of pediatrics and cardiovascular surgery. It should be of value to physicians in family practice, pediatrics, obstetrics, and cardiovascular surgery. Speakers: Visiting Faculty, Denton A. Cooley, M.D., Professor of Surgery, Baylor University School of Medicine; William Rashkind, M.D., Associate Professor of Pediatrics, University of Pennsylvania School of Medicine; William T. Mustard, M.D., Associate Professor of Surgery, University of Toronto. Yale Faculty, Norman S. Talner, M.D., Associate Professor of Pediatrics; Marie J. Browne, M.D., Associate Professor of Pediatrics; S. David Rockoff, M.D., Associate Professor of Radiology; H. C. Stansel, Jr., Assistant Professor of Surgery.

Credit: This conference is approved for six hours credit by the Connecticut Academy of General Practice

Registration fee and tuition $25.00, luncheon included (interns and residents may register without charge)

Contact: Office of Postgraduate Education, Yale University School of Medicine, 333 Cedar Street, New Haven, Conn. Phone: 562-1161 Ext. 864

GENERAL

Hartford Hospital

Saturday Mornings 11:00 a.m.

March 30

Recent Development in Pediatric Cardiology

Speaker: James Manning, M.D., Professor of Pediatric Cardiology, University of Rochester Medical School

April 6

Steroids and Fever

Speaker: Philip Bondy, M.D., C.N.H. Long Professor of Medicine, Yale University School of Medicine, Physician-in-Chief, Yale-New Haven Medical Center

April 20

Individual Versus Population Normals

Speaker: Donald S. Yoong, M.D., Chief, Clinical Chemistry Laboratory, Clinical Center, National Institutes of Health

May 18

Compensatory Renal Hypertrophy

Speaker: Bernard Lytton, M.D., Professor of Urology, Yale University School of Medicine

May 25

Clinical Interprepation of the Pediatric Electroencephalogram

Speaker: Peter H. Berman, M.D., Department of Pediatric Neurology, New York University School of Medicine.

ANNUAL MEETINGS

March 28 3:30 p.m.

New Haven County Medical Association 184th Annual Meeting

Waverly Inn, Cheshire

April 9 4:30 p.m.

Fairfield County Medical Association 176th Annual Meeting

Frederick's, Fairfield

April 10 5:00 p.m.

Hartford County Medical Association 176th Annual Meeting

Hilton Hotel, Meeting

April 30, May 1-2

Connecticut State Medical Society 176th Annual Meeting

Hilton Hotel, Hartford

June 16-20

American Medical Association 117th Annual Convention

San Francisco

NATIONAL MEETINGS

April 1-5

American College of Physicians

Sheraton Hotel, Boston

April 15-20

American Physiological Society

Ambassador Hotel, Atlantic City

April 17-19

American Surgical Association

Sheraton Hotel, Boston

April 22-24

American Association for Thoracic Surgery

Hilton Hotel, Pittsburgh

April 22-27

American Academy of Neurology

Pick-Congress Hotel, Chicago

April 25-28

American Academy of Physical Medicine and Rehabilitation

Sheraton Hotel, Chicago

April 28-May 1

American Association of Plastic Surgeons

Shamrock-Hilton Hotel, Houston

May 1-2

American Pediatric Society

Seaside Hotel, Atlantic

May 5-6

American Society for Clinical Investigation

Chalfonte-Haddon Hall, Atlantic City

May 6-9

American College of Obstetricians and Gynecologists

Palmer House, Chicago

May 11

American College of Psychiatrists

Sheraton Hotel, Boston

May 15

American Society for Gastrointestinal Endoscopy

Bellevue-Stratford, Philadelphia

May 13-16

American Urological Association

Fontainebleau Hotel, Miami Beach

May 13-17

American Psychiatric Association

War Memorial Auditorium, Boston

May 15-18

Neurosurgical Society of America

Mark Hopkins, San Francisco

May 19-23

American Thoracic Society

Rice Hotel, Houston

May 27-29

American Ophthalmological Society

Homestead, Hot Springs, Virginia

MEDICAL NEWS

Marijuana

In the United States, marijuana is the term for any preparation or extract of the Cannabis plant or hemp. Most of the active ingredients are in the resinous exudate of the unfertilized flowering tops of the plant, which can grow wild in any temperate climate. The drug is not available legally in the United States except by a special license from the Internal Revenue Service for research purposes. It has no recognized medical uses.

Marijuana is generally smoked as a cigarette but the resin is sometimes ingested in candy form, a practice most common in eastern countries. The chief active ingredient is believed to be tetrahydrocannabinol; different preparations contain varying combinations of isomers of tetrahydrocannabinol, their strength depending on where the plant was grown, the method of cultivation, how long it was stored, and the methods used in extracting the resin. At present the potency of marijuana cannot be determined by chemical analysis.

SUBJECTIVE EFFECTS—When marijuana is smoked, the subjective effects usually start promptly and last for about four hours. A dreamy state in which ideas and images flow freely and pleasantly is common. Time sense, spatial relationships and body image can be markedly distorted. There is an intensified sensory perception, especially of auditory and visual stimuli. The usual mood is one of euphoria or exaltation but there may be mood swings or even a predominant depression. Uncontrollable laughter and hilarity are common, especially when marijuana smoking is a group affair, as it usually is.

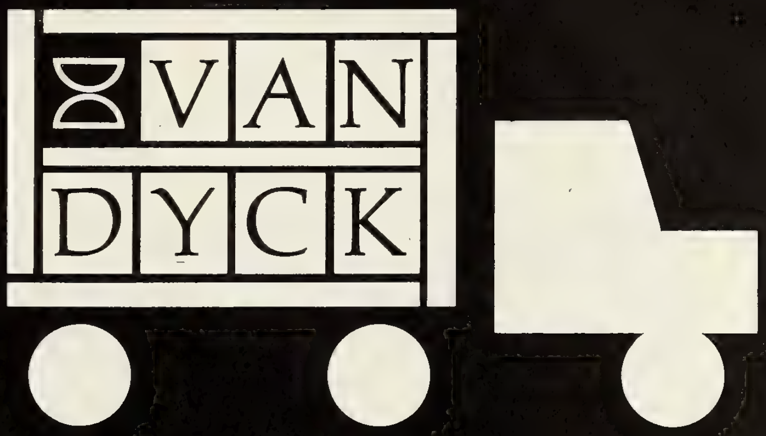
SERIOUS REACTIONS—Advocates of lifting the legal restrictions on the use of marijuana state that it is no more harmful than alcohol or cigarettes. However, reports of serious adverse emotional reactions and personality changes are increasing. Panic, gross confusion, impulsive and aggressive behavior, depersonalization, depression, and paranoid behavior have been reported, especially when marijuana is combined with other drugs, such as alcohol and amphetamines. With large doses (or in susceptible persons) delusions or hallucinations can occur (P. Dally, Brit. Med. J., 3:367, Aug. 5, 1967; E. Tylden, Brit. J., 3:556, Aug. 26, 1967). Indolence and neglect of personal hygiene may follow prolonged heavy use, and intellectual functioning and memory may be impaired. Descriptions of the behavioral and subjective effects of large doses of marijuana and of LSD (Medical Letter, Vol. 9, p. 1, 1967), mescaline and psilocybin are remarkably similar.

PHYSICAL EFFECTS—The drug sometimes causes postural hypotension. Mydriasis, conjunctival congestion and photophobia are frequent. Muscular incoordination, spasms, urinary frequency, dryness of the mouth, nausea, vomiting, and diarrhea sometimes occur. Increase in appetite is common, and has been attributed to hypoglycemia. Hypothermia has been observed and some workers have noted a Raynaud-like syndrome (cold extremities and white finger tips). Large amounts of marijuana depress respiration, which is the first sign of impending death in animals given lethal doses.

In present patterns of drug abuse, marijuana is often the first drug to be used. There is no evidence that it has any physiological or emotional effects which directly lead to more serious drug abuse, but its use may facilitate contact with persons or groups using more dangerous drugs. There has been no evidence of physical dependence on commonly available preparations of marijuana; withdrawal symptoms have been reported, however, following the use of the more potent material available in North Africa and now coming into the United States.

The hazards of occasional marijuana smoking should not be exaggerated, but attempts to limit the use of the drug remain appropriate, especially since relaxation of controls would probably lead to greater importation and use of more potent preparations with a resultant increase in serious side effects.

Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N.Y. Vol. 9, No. 19 September 22, 1968.



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Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

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Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

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Connecticut Medicine

Connecticut State
Medical Journal

Volume 32/May 1968/Number 5

STUDIES IN METABOLISM: Paul H. Lavietes, M.D., *Guest Editor*

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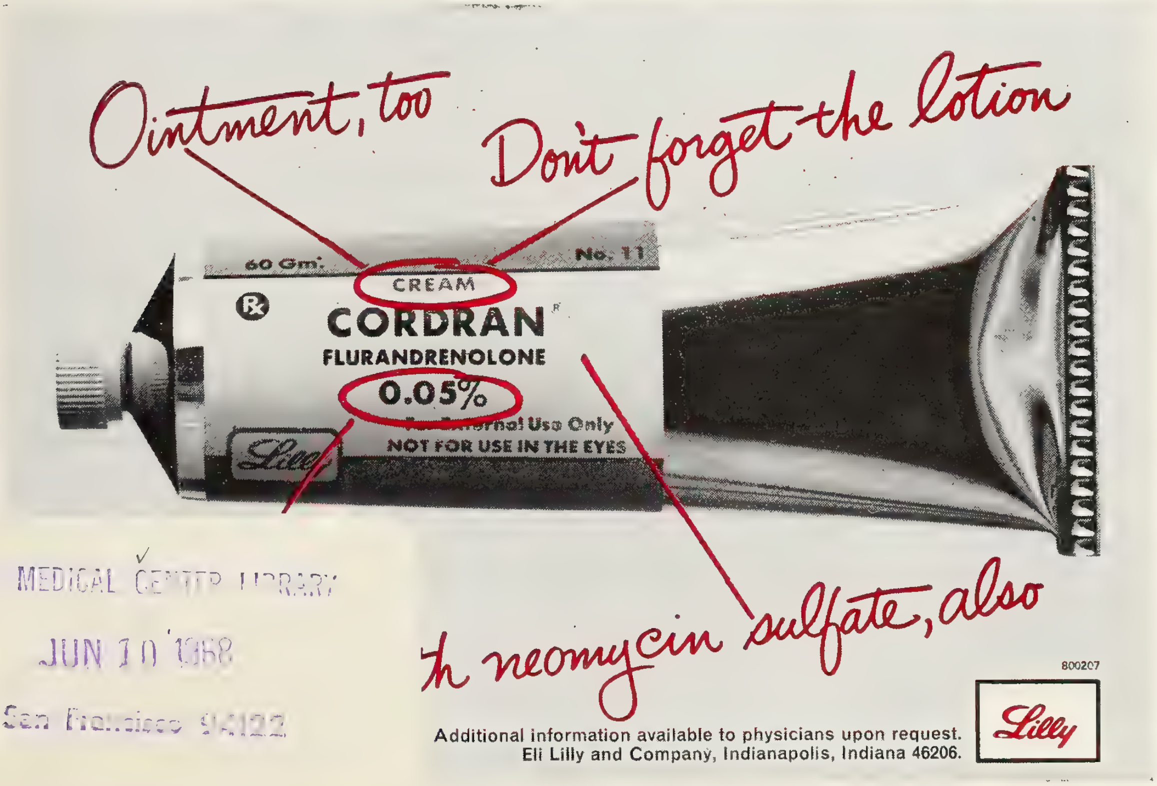

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Connecticut Medicine

MAY, 1968
Vol. 32/No. 5

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Connecticut Medicine

editorials

The Mechanism Of Action Of Oral Hypoglycemic Agents

In 1918 Watanabe[1] found that guanidine lowered blood sugar but also exhibited severe toxic side effects. The biguanides which were then developed enjoyed considerable popularity until the discovery of insulin temporarily swept them aside. Nevertheless many studies on the mechanism of action of these agents and of the sulphonureas have attempted to define their effects on normal and abnormal physiology in animals. Since human genetic diabetes differs on several fundamental ways from various animal models and systems the final understanding of the mechanism of action of these agents must come about in the patient with diabetes.

In the absence of the pancreas the sulphonureas exhibit no hypoglycemic activity. Obviously their action is presumably mediated through insulin release. In addition to insulin release, could there also be some other agency through which the sulphonureas act? In normal subjects tolbutamide increases also the peripheral utilization of glucose in addition to reducing hepatic output of glucose. The peripheral effects are not found in the diabetic patient, although the hepatic output of glucose was suppressed as in the normal person. The question then was whether tolbutamide intravenously stimulates less insulin release in the diabetic pancreas, too little to reach the peripheral circulation or whether insulin release was the same as in the normal state but its effect was dampened by the presence of insulin resistance. It turned out from studies on blood insulin by the radioimmuno assay technic that it was the presence of insulin resistance that caused a smaller and slower fall in blood glucose in the mild diabetic, even though tolbutamide causes normal or higher than normal insulin levels.

Such studies suggested that the primary action of these drugs was to stimulate increased insulin release.[2] If this were so it was asked whether their prolonged use might not accelerate the pace of beta-cell exhaustion. It was also feared that the expected "hyperinsulinism" might aggravate existing tendencies in obesity. Neither of these problems have occurred on prolonged sulphonurea therapy when the drug is taken orally.

Even very large oral doses of sulphonureas produce a much smaller rise in peripheral insulin than similar intravenous doses. A small amount of insulin is released and the bulk is cleared from the portal circulation by the liver. Consequently the drop in blood sugar observed after oral sulphonurea may be attributed mainly to the hepatic insulin effects even on normal subjects.

Histologically prolonged exposure to sulphonurea therapy induces proliferation of the pancreatic iselets both in animals and man, a kind of functional hypertrophy.[3] It is this potentiation of response to physiological insulin releasing stimuli such as glucose and aminoacids that may be responsible for the effect of chronic sulphonurea treatment in human disease. It is known that oral therapy with sulphonureas for periods of a few weeks in patients with mild diabetes enhances insulin release in response to a glucose load together with improvement in glucose tolerance.

As the results of longer term studies have become available a very interesting phenomenon has emerged; glucose tolerance remains improved despite the return to an insulin release that is quantitatively the same or lower than in the pretreatment phase. This fact has been confirmed in a longitudinal study of patients who responded to the drug. A possible explanation for these data could be that continued administration of sulphonureas affect only beta-cell function but not the degree of insulin resistance. The improved sensitivity of the beta-cell function eventually might improve to such an extent that normal insulin release would occur at normal blood sugar levels.

Acromegalic diabetes can be successfully controlled by sulphonureas. Is this due merely to increase in beta-cell function alone, or can it also be due to disappearance of insulin resistance? The end result of prolonged sulphonurea therapy whatever the mechanism appears to be improved glucose tolerance with a relatively normal insulin output after a glucose load. The initial fears of iselet cell exhaustion and hyperinsulinism due to the sulphonureas seem to have been unfounded. In fact such oral therapy for diabetes is receiving increasing interest as a possible though as yet unproved means of preventing the progression of beta-cell dysfunction in prediabetes, because of its betacytotropic or anti-insulin resistant effect or both.

The biguanides (phenformin) apparently operate through a different mechanism. In contrast to the sulphonureas, they may have an insulin-like action on many different cell membranes and structures including mitochondrial and plasma membranes. This insulin-like effect does not appear to be mediated through an increase in insulin output as measured by immunoassay. They do, however, lower the blood sugar in normal fasting human subjects because they induce an increased peripheral glucose utilization that is exactly compensated for by an increase in hepatic glucose output. In diabetics the blood sugar falls only when the peripheral utilization of glucose increased by the drug.

The results suggest that phenformin may directly diminish "requirements" of insulin in the diabetic patient. It is still unclear whether this reduction is due to better glucose utilization in the peripheral tissues or to diminution in insulin resistance. In either event the amount of insulin available from the pancreas of the phenformin treated diabetic becomes relatively more adequate to handle the metabolic task.

Wilensky and Halin[5] have recently reported some rather encouraging data which suggest that a short course of phenformin therapy may increase the frequency of remissions in latent diabetes as judged by the cortisone glucose tolerance test. The data also suggest that such a course could slow up the progression from latent to overt diabetes.

The results of successful therapy with either sulphonureas or phenformin suggest that a vicious circle exists in diabetes mellitus. Insulin resistance leads to relative insulin insufficiency which may in turn induce further insulin resistance. If this chain of events can be nterrupted relatively early in the course of the disease by oral hypoglycemic agents this may alter the course of the basic disease as well as control its symptoms. If there is primary failure with either drug it probably means that the necessary link of adequate beta-cell function in this chain of events is severely weakened at the time therapy is begun.

When "secondary failure" occurs, that is loss of control of the disease after initially successful treatment, the explanation is still unclear except there must be failure of the underlying genetic beta-cell function without which the oral hypoglycemic agents cannot perform their work. This points up the fact that the basic nature of genetic diabetes still remains a mystery.

L.H.N.

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Riots And Hospitals

Walt, et al have reported their experiences at the Detroit General Hospital between July 23-28, 1967, during a period of serious civil riot. Since the summer is coming and the threat of similar recurrences mounts as our society becomes disrupted and polarized we must learn the Detroit lesson and look to our disaster plans more carefully. Now we are suddenly aware that we must include in any big city hospital disaster plan a mechanism for ensuring function during a riot. Hospitals have long recognized their responsibility to prepare for calamities. Physicians and hospital administration have designed disaster plans calculated to enable a hospital to cope with calamities ranging from a widespread epidemic to a nuclear holocaust, to infectious diseases used as weapons.

Many things were learned from the Detroit experience that had not been anticipated. The conventional plans geared to meet an emergency of a sudden explosion or storm or transportation accident assume the presence of a uniformly co-operative and sympathetic citizenry, the immediate mobilization of all community reasources and relatively free flowing transportation. Alternative plans for nuclear disasters have been made in close cooperation with civil defense authorities. These assume widespread destruction of large areas with drastically limited communications forcing survivors and hospitals to be virtually self-supporting.

Civil riots, however, bring new problems. Casualties may arrive over a period of many days in a staccato manner. Hazardous roads between the scene of injury and the hospital may force casualties to await police or military authorities for safe

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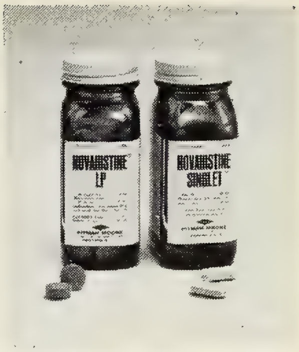

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escort. Essential hospital personnel may find it impossible to get to work and others already at work in the hospital may have similar difficulty in returning home for a number o fdays being forced to work around the clock without rest or sleep as casualties come in. Patients with minor injuries must be rapidly treated and discharged, but this may not be easy to accomplish if the hospital is situated close to the area of violence. The hospital may need to admit large numbers of persons and innocent victims of violence and simultaneously provide for the security of both groups. Finally it has become vital to the hospital itself that its personnel be adequately protected from outside attack as happened in Detroit. It appears then that provision must be made for these factors in the usual disaster plans.

The casualties in Detroit resulting from a major civil disturbance occurred in an atmosphere of marked emotional tension in which there was disruption of normal social mores and a disregard for the law. This seriously affected the operations of the hospital which was called upon to provide care for these patients. The most difficult aspects Walt found concerned the safe transportation of patients through the troubled areas. Ambulances and unguarded vehicles are likely to be attacked and need armed protection from the police. Other parts of the hospital had to be guarded also, since violence may break out within the building.

The incubation period of a serious civil disorder provided a few hours of warning which allowed time for the full mobilization of hospital physicians, administrators, nurses, technicians, orderlies, cooks and others. One necessity was a triage officer, a physician who examines every incoming patient and determines priority of treatment, based on the seriousness of the injury and the facilities available. This triage officer should possess "broad medical knowledge, an equable temperament, sound judgment, a large commanding voice and physical stamina."

Stamina became a problem for every member of the hospital staff. Because the length of a disturbance cannot be predicted and the staff can't get home for rest, regular rest periods must be established and enforced otherwise many physicians, nurses and others will tend to overestimate their physical reserves. The staff in Detroit dealt with 1,475 patients during the emergency and during the busiest 36 hours 456 were treated, enough to exhaust any team without preparations for rest. However, the patients treated during the emergency did not have unusual injuries. The wounds caused by gunfire, stabbing and beating were well within the competence of the staff.

The major difference between handling such injuries and the situation in Detroit was the fact that the hospital itself was part of the hostile environment. Apathy or even obstruction replaced the usual reactions of citizens on the streets to the work of the ambulance crews. Physicians, nurses, all hospital staff had to risk personal injury or death to reach home or return to the hospital. Within the hospital it suddenly became important to be aware of the potential danger of placing a rioter in the bed next to a police officer or an injured bystander. As a result, wounded, angry combatants from both sides of the fight had to be treated, guarded and protected.

The problem was very real. It could again appear soon and often. All those responsible for hospital preparedness will find the report from Detroit thoughtful and provocative, for there the organized medical teams did a heroic job in an uncharted area of civil disorder.

L.H.N.

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Medical Uses Of Lysergic Acid Diethylamide (LSD)

The debate about the advantage and dangers of LSD continues unabated. The alleged benefits when the drug is taken indiscriminately and under uncontrolled circumstances are nowhere substantiated. On the contrary objective data now strongly suggest that the claims of augmented esthetic sensitivity and creativity cannot be confirmed by intensive psychological testing.[1] Similar criticism can be levelled against the statements regarding unusual insight achieved after the use of the drug. The claims regarding the ability to love may well reflect LSD induced increase in passivity and decrease in aggressiveness rather than a true augmentation in capacity to give, accept or appreciate love. The aphrodisiac potential of LSD appear to be clearly spurious. It is probably true that many of those who take LSD experience enormously erotic thoughts and hallucinations, but only rarely are these transplanted into actual behavior. This, of course, makes LSD actually an anti aphrodisiac.

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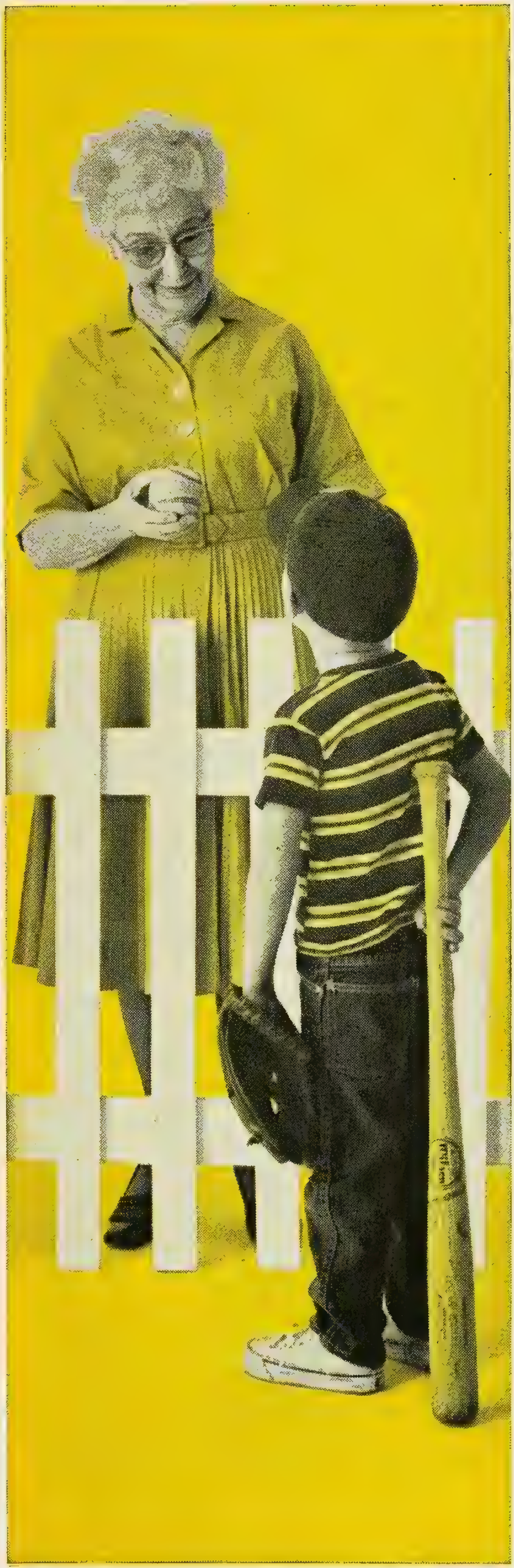

The drug does, however, have remarkable pharmacologic and biochemical actions probably arising from antagonism of serotoin action and consequently could have some potential uses provided it were administered under carefully controlled conditions by qualified skillful clinical pharmacologists. The beneficial results reported so far, but badly in need of confirmation devolves around its use in alcoholism, psychoneuroses and its potent analgesic properties in patients with widespread cancer complicated by pain.

In alcholoics, LSD given on one to several occasions together with supportive and rehabilitative techniques results in abstinence or striking redution in alcoholic intake up to four years in one-quarter to one-half of patients.[2] These results are encouraging but inadequately controlled and need careful validation and long term follow-up.

In psychoneuroses LSD may be a valuable adjunct to psychotherapy in certain neuroses especially those characterized by compulsion and phobias. In carefully selected patients the drug can "surface" depressed material and effect more rapid transference between patient and therapist. A single LSD session may uncover so much new and important information that it may take months or even years to analyze and interpret it. The drug has also been claimed to be beneficial in the treatment of some autistic children whose psychoses have resisted other available treatment.[3] Psychopathics are at times said to benefit from LSD treatment but the data again are grossly inadequate.[2]

In the psychoses, LSD is ordinarily considered to be contraindicated.[3] Even in the best of circumstances, some of the patients treated suffer severe and prolonged exacerbations. This also points up the dangers if the drug is taken promiscuously since many such are psychopaths and suffer already from psychosis. Louria[1] describes acute psychosis, acting out of psychopaths, or homosexual impulses, inadvertent or intentional suicide attempts, convulsions, uncontrolled aggression, and overwhelming ego-shattering panic reactions. However, these experiences happen to very few normal persons when the drug is taken under medical supervision.

It is important to recognize that none of the medical uses of LSD listed above are adequately documented. For each a great deal more research is needed. Unhappily as a result of the untoward publicity there has occurred a drastic reduction both in available research funds and the number of involved investigators. In 1964, approximately 70 investigators were studying LSD in the laboratory and in man. By 1966, before knowledge about chromosomal damage, there were only 17 investigators who received $927.000 in funds. In the projections for 1968 there are eight investigators and $547.000 in federal research funds.[5]

The influence on society as a result of indiscriminate use of LSD can be profound. Prolonged psychosis and hospitalization, prolonged panic reactions, bewilderment and fear lasting for weeks or months, chronic withdrawal from real life leading to permanent drop outs from society, abjuring family, friends, productive activity can be a great burden on society. When many people embrace a hallucinogenic oriented unproductive existence, the burden on family and others can reach boundless proportions. Then there is the documented chromosomal breaks in 80 per cent of LSD takers. What the permanent genetic damage may be in infants born of mothers who took LSD during early pregnancy is awesome. [6] [7] Experimental studies on pregnant rats or mice early in gestation who were given LSD showed an abnormally high proportion of embryologic abnormalities and stillbirth.[8] If the drug can produce chromosome abnormalities it certainly can also produce neoplastic changes in the user.

It is clear then that the potential medical uses of LSD could be considerable while the claimed benefits taken under uncontrolled circumstances are dangerous beyond peradventure. We must do everything to counteract the psychedelic missionaries from enveigling young people into joining the hallucinogenic drug movement. For widespread use of LSD could lead to a whole generation of psychedelic drop outs incapable of and uninterested in addressing themselves to the important sociologic problems that challenge our times.

Good news comes to us from the FDA that there is a decline in the general use of LSD around the country. We must not be too quick to conclude that this is the result of young people heeding scientific reports on the dangers in taking the hallucinogenic drugs. Scientific reports about smoking have done little to influence the habit among the populace. Perhaps young people, instead of retreating from reality are beginning to come to grips with the disorganizing influences of war, inflation, decayed cities and other serious conditions in our society. The older generation has bequeathed them these problems apearently themselves unable to do anything about them. If the young gen-

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Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

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Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease; impending hepatic coma from thiazide-induced hypokalemia.

Warnings—Patients: 1. No other drugs (particularly "cold preparations" and antihistamines), cheese or alcohol without physician's consent. 2. Promptly report orthostatic symptoms, severe headache, other unusual symptoms. 3. Angina pectoris or coronary artery disease patients must not increase physical activity with improved anginal symptoms or well-being.

Physicians: 1. Use antihistamines, hypnotics, sedatives, tranquilizers and narcotics (meperidine contraindicated) cautiously in reduced doses. 2. Stop Eutron two or more weeks before elective surgery; in emergency surgery reduce premedication (narcotics, sedatives, analgesics, etc.) to 1/4 to 1/5; carefully adjust anesthetic dosage to patient response. 3. Use cautiously in advanced renal failure. 4. Pargyline may induce hypoglycemia. 5. Consider possible sensitivity reactions when a history of allergy or asthma is present. 6. If potassium is indicated, dietary supplement is recommended; enteric-coated potassium tablets may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation frequently requiring surgery; discontinue medication immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occurs; Eutron does not contain added potassium. 7. Possible systemic lupus erythematosus has been reported for thiazides.

Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804438R

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eration can be made to become involved in such causes, they will not easily be led to retreat from them through psychedelic hallucination.

L.H.N.

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Nutrition And Osteoporosis

Osteoporotic bone loss is a health problem of major magnitude. It is not just the problem of fragile inactive elderly people. It is a world wide problem and we are now revising previous notions about its cause. It appears that bone loss is a general phenomenon beginning by the fifth decade in both sexes and progressing more than twice as fast in the female as in the male. The sequelae of osteoporotic bone loss are known to all as we recognize that 4.5 million contemporary American women suffer from hip fractures, vertebral decalcifiation and even collapse of some of the vertebra. Possibly we may be less cognizant of the serious nature of alveolar bone loss leading to diminution of tooth support, fenestration of the roots and actual loss of teeth.

Clinical investigators increasingly acknowledge the likelihood of a pleurocausality for osteoporosis. The question, of course, arises how the observations made in clinical surveys and field studies, are applicable to the growing problem of symptomatic osteoporosis as encountered in medical practice. Is the causality of the near universally occurring or normal bone loss in our adult societies different in any way from that which underlies those that develop fractures for example.

Bone is formed by osteoblasts and destroyed by osteoclasts.[6] These cells from a metabolic barrier so to speak on either side which controls the formation and destruction of bone. We know very little about what controls these processes. Ordinarly the controlling mechanisms in the normal animal in rate of bone formation and destruction are somehow maintained in reasonable equilibrium. But bone destruction is not the reverse mechanism of bone formation and the general idea that one can force bone formation by an increase in supply of structural materials, such as protein and calcium and thus counteract bone destruction, is probably invalid.

Garn[1 4] points out that calcium intake does not relate to bone loss either on a population or on an individual basis. Intake of 1500 mg. calcium per day do not seem to protect and levels as low as 300 mg. per day do not seem to contribute to bone loss. To be sure in exceptional cases such as gastrectomy, lactose deficiency or malabsorption syndromes, bone loss is accelerated, but in people taken on mass, neither low calcium intake nor high phosphorus seems to lead to osteoporosis. Such findings cast doubt on the original low calcium hypothesis. They raise questions as to the allegedly bone protecting nature of high calcium diets and the presumed therapeutic value of 1.5 grams of calcium per day.

Most people actually take in enough calcium in the diet to maintain appropriate calcium balance and yet there is an irreversible daily loss of 30 mg. of bone calcium after the age forty. Balance studies reveal that the skeleton is inevitably losing 900 mg. calcium a month, nearly 9 grams a year and 450 grams over a 5 decade period in the female. What then is the best protection at present against osteoporosis? To be sure those individuals born with a heavy skeleton will reach the critical point of skeleton depletion much later than those with a light skeleton and will show the clinical concomitant later in life. But the problem still remains.

Bone loss progresses twice as fast in females as in males beginning by the fifth decade. This suggests that in addition to the aging process, deficiencies of hormones may be very significant. Smith[5] believes deficiencies of anabolic hormones, particularly androgens estrogens and possibly growth hormones may be operative. This problem needs much further study than has been given to it. We know that there is regression of bone mass which parallels the equally universal decline in hormones which retard bone resorption. The greater the departure from normal mineral metabolism or endocrine function, the greater will be the addition to the normal process of bone loss. Clearly when of extended duration, even subtle departures will be causal to the more severe osteoporosis encountered in clinical practice.

There is an individual element also in the bone loss problem. Females seem to have a lesser bone mass. It is more of a liability to those who have a smaller absolute bone mass problem to begin with and more of a hazard to those who lose bone more rapidly. The word osteoporosis is almost an inadequate descriptive term because it leaves out the time factor and does not consider different kinds of osteoporotic bone loss. The fact is that bone loss is also a problem of individual bones.[3 4] Bone specific differences in loss rate pose an intriguing problem. Within a bone, breaking strength may increase at mid shaft, yet increase at the epiphyseal ends and in the femor decrease markedly at the femoral neck.

In clinical studies patients with osteoporosis and Paget's disease have been treated orally with fluoride. In the main the results suggest a decrease in calcium loss and many cases indicate relief of symptoms.[2 7] The bone mineral has been stabilized in vivo by fluoride substitution and crystal growth. We know that the rates of osteoporosis and periodontitis are lower in areas where the water supply is high in fluoride as compared to lower fluoride areas. Posner[2] points out that an increase in percentage of crystallinity tends to stabilize the hard tissue against biochemical dissolution. Whether this occurs because fluoride retards osteoclastic activity has not been studied.

However, prevalent adult bone loss may be, and seemingly inexorable, yet it should not be inevitable. We already know that fluoride promotes crystal growth of the apatite phase in bone, producing a more stable mineral phase. Evidence continues to mount that fluoride consumption may be an important factor affecting the development of osteoporosis. Certainly future studies upon the prevention or epidemiology of this disease must include consideration of fluoride consumption. Since prevention is clearly more desirable than treatment, the need for studies which adequately define the requirements for fluoride and its effects under a variety of environmental conditions is clear. We also know that vitamin D deficient rachitic bone leads to an apparent lack of maturity, the bone mineral is less crystalline and more amorphous.

We now have two models of major bone disease resolved by nutritional understanding. Its time we recognized osteoporotic bone loss as a health problem of major magnitude and pursue its solution with the same energy and perserverence as we are now attempting in prevention of other diseases as heart disease and cancer.

L.H.N.

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The Connecticut Regional Medical Program (CRMP)

The focus is on the patient; the mechanism is cooperative arrangement. The emphasis is on local initiative—flexibility and decision making . . . reason for the program is the relationship between Science and Service.

On October 6, 1965, President Johnson signed P.L. 89-239 which made provision for regional medical program planning and implementation to set up regional centers for the prevention, treatment and rehabilitation of patients suffering from heart disease, strokes, cancer and allied disorders. On February 1, 1968, Dr. Henry T. Clark, Jr.,[1] Program Coordinator of the Connecticut Regional Medical Program (CRMP) presented his report of the activities up to date.

The basic philosophy of CRMP is to provide optimal patient care in the above diseases. The care of the patient is said to be the common end product and is the base on which CRMP had brought together for planning purposes various elements of the health systems of this state. The care of the patient is said to require a way to insure the delivery of comprehensive, high quality medical care to the entire population of Connect-

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icut. Implied in this ideal is "completeness, integration of prevention with treatment and rehabilitation, fostering active promotion of health and education for it, maximizing availability and accessibilty of qualty care provided on a multi professional basis and in a personalized manner."

Obviously regional coordination is the necessary organizing mechanism for realizing of this ideal and because Connecticut has two universities, thirty-five regional hospitals, good highways and a goodly amount of physicians and dentists and many volunteer agencies, no new additional facilities need to be created at the beginning and the state appears to be an ideal for pilot experiments in this field.

The first requirements seemed the need to identify and organize various elements of the health care system in the state. There would need to be sustained planning within the ten subregions into which the state is divided. Finally to work out arrangements required the complex coordination between community hospitals, various extended care facilities and programs, the public and voluntary health agencies and most important the community based practicing physicians. The CRMP seeks ways in which the two university medical centers and major resources of Connecticut can best make available their specialized skills and reinforce physicians and institutions that render care at the local level.

To accomplish all this investigation and planning will require money. First will be the need to stimulate and assist development of subregional health planning of overall programs for personal health services. There is intended the development of one or more demonstration programs linking hospitals, nursing homes, home health services and rehabilitation centers. Then a series of patient care workshops are comtemplated to explore the need in local communities for continuity of patient care and to discover the ways in which this need can be met.

To accomplish this the CRMP encourages creating a working partnership between hospitals and the university and the creation of a "third faculty" consisting of "full time chiefs" of services in selected hospitals around the state who would spend part of their time in university centers. Clearly the idea of this third faculty would be to assist in training interns and residents, to help continuing education of the practicing physician as well as assisting in management of selected patients. This faculty is conceived as aiding in development of specialty services and finally to help funnel difficult to manage cases to the university center.

Another way of spending the money is to help in development of ways to render certain specialized and technical services to the patient and the physician. The many new developments in diagnosis and treatment that require scarce and highly skilled personel such as coronary care units, high energy radiation for victims of cancer, regional reference laboratory, medical and allied library resources and services, will be made available.

Another way of spending the money will be in assembling and analyzing the data on the medical care program. How is health care organized and delivered? This should clarify in the minds of the doctors the various forces which are shaping the practice of medicine. The idea further is that a partnership between organized medicine and the "prime" researchers in public health will lead to a charting of a broad course of research and then help to carry out the conclusions into practice.

Finally is the idea among the CRMP that an operating grant should be obtained for financing health care. The trouble with this is that we need to know costs of operating the present system of medical care, costs of regional medical planning and programming to help chart a definitive course of action. Nor do we know what it would cost if certain schemes are devised when they are carried into operation. CRMP thinks that if we had a professor of Health Economics at the University that such research could be carried out most effectively.

What has come out so far is that CRMP is searching for a concerted course of action to develop a coordinated medical care system for Connecticut. While it is primarily concerned with strengthening and improving the regions capacity to deal with heart disease, cancer, stroke and allied diseases, it aims to contribute to the improvement of the whole medical care system.

It is probably true that the citizens of this country want a health program which can provide comprehensive quality services with a heavy emphasis on prevention. They also want compassionate personalized care. The medical profession must stand guard to assist in the first requirement and actively depend on the second. Only with the medical profession's help will the CRMP become a boon instead of a boondogle.

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New Light On Peptide Hormones

The role of a hormone in the body can be elucidated by methods which permit us to follow the fluctuations of the hormone content in the plasma since this makes it possible to evaluate secretory regulation. To measure the concentration of hormones in the plasma, a wide variety of techniques have been developed. First was the direct clinical extraction for measuring steroid and thyroid hormones. Here one takes advantage of the unique possession of iodine by the thyroid or of certain special properties of solubility and chemical configuration of the steroids.

The peptide hormones, however, do not possess such unique characteristics that allow them to be distinguished chemically from the remainder of the serum proteins which are present at a million to a billion times higher concentration. The classic methods hitherto employed were testing hormone effects of the plasma on a living system or in vitro and comparing the response with that of a standardized preparation of the hormone. This has not been sensitive enough and consequently many workers were led to investigate other means of measuring these hormones. Now the radioimmunoassay method has been perfected and has made it possible to obtain accurate values for peptide hormones in body fluids and to study their production, metabolism and degradation in the body.

We can now classify the peptide hormones in a functional way. There are the metabolic hormones such as insulin, glucagon, ACTH and growth hormone, all of which are concerned with fuel meabolism, while TSH influences general metabolism of cells through stimulation of thyroid hormone production. Parathyroid hormone and calcitonin are regulators of calcium metabolism. Vasoactive peptides—vasopressin, renin and angiotensin regulate arterial pressure. Then there are a miscellaneous group such as erythropoietin which stimulates red blood cell formation and the melanocyte stimulating hormone.

Some of these hormones exhibit their effects within a few minutes such as insulin and glugagon which are thought to act at the cell membrane and influence activity of a membrance bound enzyme, adenyl-cyclase which has a wide variety of metabolic effects. Some hormones act more slowly such as growth hormone also acting at the cell membrane but are slowly acting because their effects depend upon new protein synthesis and this is why their effects can be blocked by agents that interfere with protein synthesis.

Some of the peptide horomones; glucagon, insulin, growth hormone and ACTH may at times be acutely stimulated by the proper physiological factor. This stimulation may result in an increase in the plasma hormone concentration by 10-20 or even 50 times. This behavior is in marked contrast to the much smaller fluctuations generally observed with the thyroid and steroid hormones. After the rise in the plasma concentration to very high levels and the hormone has had its desired effect, it is rapidly disposed of by metabolic degradation. In general, Berson points out that the half-life of the peptide hormones range from 15-45 or 60 minutes. By contrast the thyroid hormones have a half-life of 2-7 days.

Insulin levels rise rapidly after intravenous glucose for 30 minutes and them fall rapidly after discontinuance. For insulin this type of behavior has an obvious advantage. The hormone is called forth on need and is allowed to disappear very quickly after removal of the stimulus (when the blood sugar goes down). If this did not happen one would be frequently exposed to the hazard of hypoglycemia as a consequence of persistently high plasma insulin concentrations even after its need has passed and the blood sugar has fallen. The same is true for ACTH and also for TSH. The short half-life of peptide hormones seem an experimental fact.

The second general characteristic of the peptide hormones concern their state in the plasma. Cortisol are bound to several plasma proteins. It was but natural to carry over this concept to peptide hormones and to suppose that they also are bound to plasma proteins. This view has been proposed for insulin, growth hormone and ACTH. But after careful study, Berson has concluded that neither insulin nor growth hormone and perhaps none of the peptide hormones can be thought of as being bound to a normal serum protein.

As a result of the radio-immunoassay technique we have learned a great deal about insulin action and have disposed of Mirsky's view that in some diabetics the problem is due not to deficient insulin secretion but rather to an accelerated destruc-

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Precautions: Some individuals may experience drowsiness, anorexia, and slight gastric distress. If excessive drowsiness occurs, it may be necessary to increase the interval between doses. Persons on full dosage should not operate any vehicle. Use may result in overgrowth of nonsusceptible organisms. If infections appear during therapy, appropriate measures should be taken. Infections caused by beta-hemolytic streptococci should be treated for at least 10 full days to help prevent rheumatic fever or acute glomerulonephritis. Use of tetracycline during tooth development may cause discoloration of teeth.
Adverse Reactions: Gastrointestinal—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes (a case of exfoliative dermatitis has been reported); photosensitivity; onycholysis and discoloration of nails (rare). Kidney—rise in BUN, apparently dose related. Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. In young infants, bulging fontanels following full therapeutic dosage has been reported. This has disappeared rapidly when drug was discontinued. Teeth—dental staining (yellow-brown) in children of mothers given tetracycline during the latter half of pregnancy and in children given the drug during the neonatal period, infancy, and early childhood. Enamel hypoplasia has been seen in a few children. Blood—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. Liver—cholestasis (rare), usually at high dosage. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy.

Lederle
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tion of insulin by an enzyme insulinase which is presumably distributed throughout the body. By labeled insulin, Berson found that in most diabetic patients insulin was being destroyed less rapidly and that this strange phenomenon was due to the presence of antibodies to the insulin with which diabetic patients were being treated. As a result the insulin was bound to the circulating antibody and this prevented insulin from rapidly passing the capillary wall. In the diabetic who had not been treated with insulin, Berson could not detect any difference in disposal of insulin between diabetic and non-diabetic patients.

Apparently there is no binding of insulin in anyone who has not been treated with that agent. In everyone treated with exogenous insulin continually for several months or longer there develops such binding. Even for some years after discontinuance of treatment one frequently finds insulin antibodies in such patients. An explanation for increased insulin resistance secondary to infection is now known to be a rapid increase in antibody which binds insulin and reduces greatly its effectiveness.

Berson points out that diabetic patients can retain a relatively high concentration of plasma insulin even in the fasting state, simply because these patients are trapping the insulin with antibody. However, the antibody bound insulin is not biologically effective so that the blood sugar continues to rise until enough free insulin is present to maintain the blood sugar at levels that do not further stimulate the iselet cells.

It may be that when synthetic insulin of the same chemical configuration as human insulin becomes available, then antibody to insulin will not form and our control of diabetes will be greatly simplified. Then we will not have to contend with the diabetic requiring hugh amounts of exogenous insulin because of his developing growing amount of antibody that binds the insulin and makes it biologically inert. We thus have now the explanation for the diabetic who requires large amounts of insulin and yet is unable to avoid hyperglycemia and glycosuria.

L.H.N.

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Race And Lactase Deficiency

There is a good correlation between intestinal lactase deficiency and milk intolerance. Those who are deficient in this enzyme develop bloating, cramps and diarrhea within two to four hours after ingestion of lactose in the form of milk. The reason is that such patients cannot break lactose down into its constituents glucose and galactose which are readily absorbed, whereas the lactose itself is not absorbed but acts as an irritant to the bowel. If lactose is administered to such patients then besides the intestinal symptoms there is no glucose for absorption and no rise in blood glucose levels.

There are three possible explanations for this lactase deficiency; an inherited trait, an adaptation to the decreased ingestion of milk in adulthood or perhaps as a result of some intestinal injury. The answer to this problem would be forthcoming if we knew the incidence of this deficiency in the general nonpatient population.

One such study has come to us from Uganda where Cook and Kajubi[1] found an incidence of 72 per cent of lactase deficiency in African negroes. Both males and females were equally affected. Milk drinking after weaning is very unusual in the area of central West Africa whence the American negroes came. Their ancestors drank no milk because the tsetse fly borne trypanosomiasis makes raising dairy cattle virtually impossible in this section.[2] These lactase deficient people therefore had less need for intestinal lactase after infancy. There therefore appears to be a correlation between milk ingestion and lactase in the intestinal tract.

Animals also generally do not consume lactose after weaning and there occurs a decrease in lactase activity[3]. One animal the California sea lion does not even have lactose in its milk, has no need for intestinal lactase and has no intestinal lactase[4].

Bayliss and Rosensweig[5] proceeded to study a prison population for the presence of milk intolerance and lactase deficiency. The study was conducted on 40 healthy non-patient volunteers, 20 colored and 20 white. As might have been expected from the African studies 19 of the 20 negro volunteers had a history of milk intolerance which began during or after adolescence. Only two of the 20 white volunteers suffered from milk intolerance. The clinical features were similar; abdominal distension, 30-60 minutes after milk ingestion, then passage of loose watery stools 2 hours after drinking 1-2 glasses of milk. It is interesting that the de-

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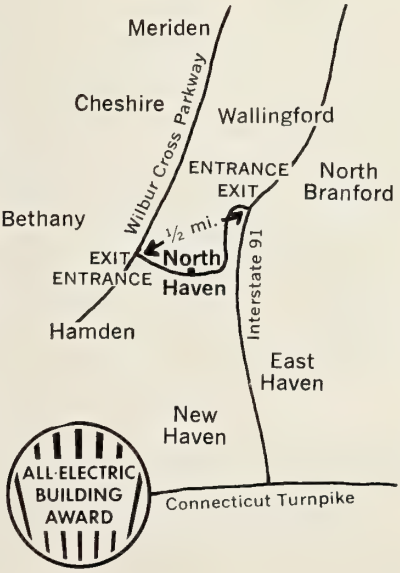

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gree of lactase deficiency varied, since the symptoms of intolerance in 6 of the subjects only appeared if they drank 1 quart of milk. Most of the intolerant subjects had no aversion to milk but learned to restrict their intake to less than 1 glass a day extolling its virtue as a producer of "regularity".

The confirmation of intestinal lactase deficiency came from studying the subjects lactose tolerance tests and from intestinal biopsies. The histological examination of the intestinal biopsy ruled out possibility #3, in causation of milk intolerance, because the cells lacked lactase but were otherwise normal.

The marked racial differences between white and colored subjects in their intestinal lactase content suggests of course that the level of enzyme activity is genetically controlled. Inherited deficiencies of lactase, invertase, and isomaltase causing severe diarrhoea have been reported in a small number of children and adults and this lays the basis for the concept of a genetic control of lactase levels in the general population. A family history of milk intolerance has been obtained from some adults with lactase deficienyc.[6] Most inherited enzyme deficiencies including inborn errors of metabolism are recessive traits and only appear in the individual homogygous for the trait. Perhaps this is the reason Bayliss couldn't establish family preponderance of lastase deficiencies in the subjects in their study.

There thus appears to be 2 populations, one which maintains high intestinal lactase levels into adult life and another in which lactose was consumed without symptoms during childhood but in which lactase levels become low when evaluated during adulthood. The question arises why milk intolerance appears at the time of puberty or late adolescence. Can there be two kinds of lactase, one in childhood which disappears as it does in animals and a second in adulthood which is either not present at all in these patients or fails prematurely. The answer to this question must come from further study. The differences between the milk tolerant and intolerant groups could not be attributed to amounts of milk ingested before the lactase deficiency appeared. Enteritis was not found. The subjects also had no intolerance to other foods and no irritable colon syndrome.

It is interesting that the lactase deficiency had not become clinically significant to these subjects because all had learned to limit their milk intake to amounts which could be tolerated which was usually a glass of milk or less per day. As noted above several learned to use milk as a laxative.

It is important for the physician to anticipate and to recognize milk intolerance since it occurs so frequently in the colored population and in 10 per cent of the white population of this series by Bayliss. It is especially important to recognize in pregnant women and persons with peptic ulcer who consume large amounts of milk One should also recall that milk intolerance may have sociologic significance since some welfare programs provide powdered milk for impoverished recipients, many of whom are negroes and who might be expected to have deficiency in intestinal lactase. And we must not forget about the powdered milk we send abroad especially to african populations.

When lactose is fermented as it is in cultured buttermilk, acidophilus milk and yogurt, it contains almost no lactose and lactase deficient persons should be able to consume milk in these forms without untoward effects.

L.H.N.

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Medical Cure Of Thyrotoxicosis

When something goes wrong with the normal homeostatic mechanism governing thyroid hormone production, we may get hyperthyroidism. It is also possible that some abnormal force is operating beyond its control, otherwise hypersecretion of thyroid hormones would quickly be turned off and the disorder correct itself. If we understood the basic abnormality it might open the way toward prevention or correction by rational means. We do not yet know the cause of hyperthyroidism, but we have enough understanding of the disorder based on facts well known to successfully treat it without resort to the knife and other measures destructive of tissues. This is the thesis presented in the Billings lecture by Dr. Howard.[1]

As far back as 1889, Hutchinson[2] wrote that hyperthyroidism will spontaneously regress if given sufficient time and the patient does not die of the disease in the meanwhile. In the pre-iodine days when surgery was so hazardous, rest homes were set up. If they retained their clientele for five to ten years then in a high proportion of cases, if death did not supervene, a remission occurred in a high proportion of cases and they could then resume their normal lives. When Plummer[3] introduced iodine as a preoperative measure, surgery became the method of choice for treating hyperthyroidism and the idea of probable spontaneous recovery receded into the background.

The third era in the management of thyrotoxicosis was ushered in by the introduction of thiourea and its derivates in the early 1940's by Astwood.[4] The drug inhibits thyroid hormone synthesis. Nowadays, the use of one of these blocking agents is almost always the first form of therapy even if surgery or radioactive iodine is planned subsequently. The chief agents used propylthiouracil and methimazole exhibit a low rate of toxicity manifested largely by sensitivity phenomena, skin rashes, serum sickness and granulocytopenia. In 100 cases Howard encountered but one case of sensitivity and then only to one and not the other of the blockers. Others have reported 5 per cent. Furthermore, if a patient proves sensitive to one drug the other agent may be tolerated with impunity. Since most reactions occur in the first 25 days one can continue their use with security quite indefinitely thereafter.

Studies from all over the world have shown amazing uniformity with the use of these blockers. There is equally uniform agreement that when thyrotoxicosis has been controlled by such agents for six months to a year and the drug is then withdrawn, there will be recurrence of the disorder within a few months in about half the cases. This finding holds true whether the drug is withdrawn gradually or abruptly and whether the patient has become hypothyroid during this period or not. Most significant is the fact that half of the patients do not relapse and the rcent report by Hirshman, et al[5] over a follow-up period of fifteen years bears out these findings.

The philosophy behind treatment then is to control the disease for a lifetime if need be with a drug such as prophylthiouracil until spontaneous remission occurs. By lowering the dose of the drug when hypothyroidism develops and raising it if

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hyperthyroidism recurs. Hirshman and his group controlled the disease this way but the patients seemed to be insecure moving between the discomforts of too much or too little circulating thyroid hormone.

This dilemma Howard overcame by gradually administering thyroid to full replacement dosage (2-3 grains daily) once thyroid production was blocked by the antithyroid drug. With this regimen he was able to maintain the patients in a steady state of euthyroidism and they were so satisfied that they were reluctant to test out whether or not a spontaneous remission had occurred. However, if a spontaneous remission had occurred then the patients were free from medication from then on. And so the question arose, how should one determine whether such a remission has in fact occurred and if recovery from the disease has occurred, then what?

To determine the presence or absence of a well established recovery, Howard withdraws the blocking agent and continues the thyroid dosage. After five days if a complete remission has occurred the ^{131}I uptake will be minimal. Thus far fourteen of his patients were in this category. The uptake was barely perceptible, the gland was small and no signs of vascularity were detected by palpation and there was no return of thyrotoxicosis. Some of his patients have gone for eight years, others for eighteen months. Three have gone through pregnancy. But all have continued to take 2-3 grams thyroid daily.

The final question is what to do with the patient if a spontaneous remission has been established. If the patient has Graves' disease with an uncontrolled excess of thyroxin not due to excess of thyrotropin, the size of the thyroid will shrink with propylthiouracil alone, and the recurrence rate when the drug is discontinued is far lower than in those in which increase in the size of the gland occurs during therapy. Those in whom the gland enlarges with treatment are considered to have increase in thyrotropin and it is in these that thyroid extract therapy may be expected to "shut off" thyrotropin production by the pituitary gland.

Such observations would favor the administration of thyroid extract after remission of thyrotoxicosis has been achieved. To stop both drugs might compel the intrinsic mechanism to take over and manufacture thyroid hormone through release of thyrotropin. "Let sleeping dogs lie" says Howard and simply continue to provide thyroid hormone exogenously. In over 100 patients, Howard found good cooperation to continue this regimen. No patient experienced progression of ocular symptoms since therapy was begun. There may be one who might do this and only then is operation indicated.

The final question is what does one do with the patient who cannot take either of the blocking agents because of sensitivity. Most can take one if sensitive to the other. If sensitive to both, we are reverted back to the Plummer era, iodine preparation and then surgery.

At some future date when the cause of thyrotoxicosis becomes clear we may with equal safety attack the cause. At present there is no harm in the procedures outlined, either theoretical or so far in fact. What is expecially helpful is that the treatment can be carried out without resort to any of the elaborate diagnostic procedures. It can be carried out with minimal risk and with complete comfort to the patient once the initial thyrotoxicosis is controlled.

The patients that will need surgery are now very few and far between, the rare case in which ocular signs progress, the rare case that is sensitive to both blocking agents. In practice thyrotoxicosis is now a medical problem.

L.H.N.

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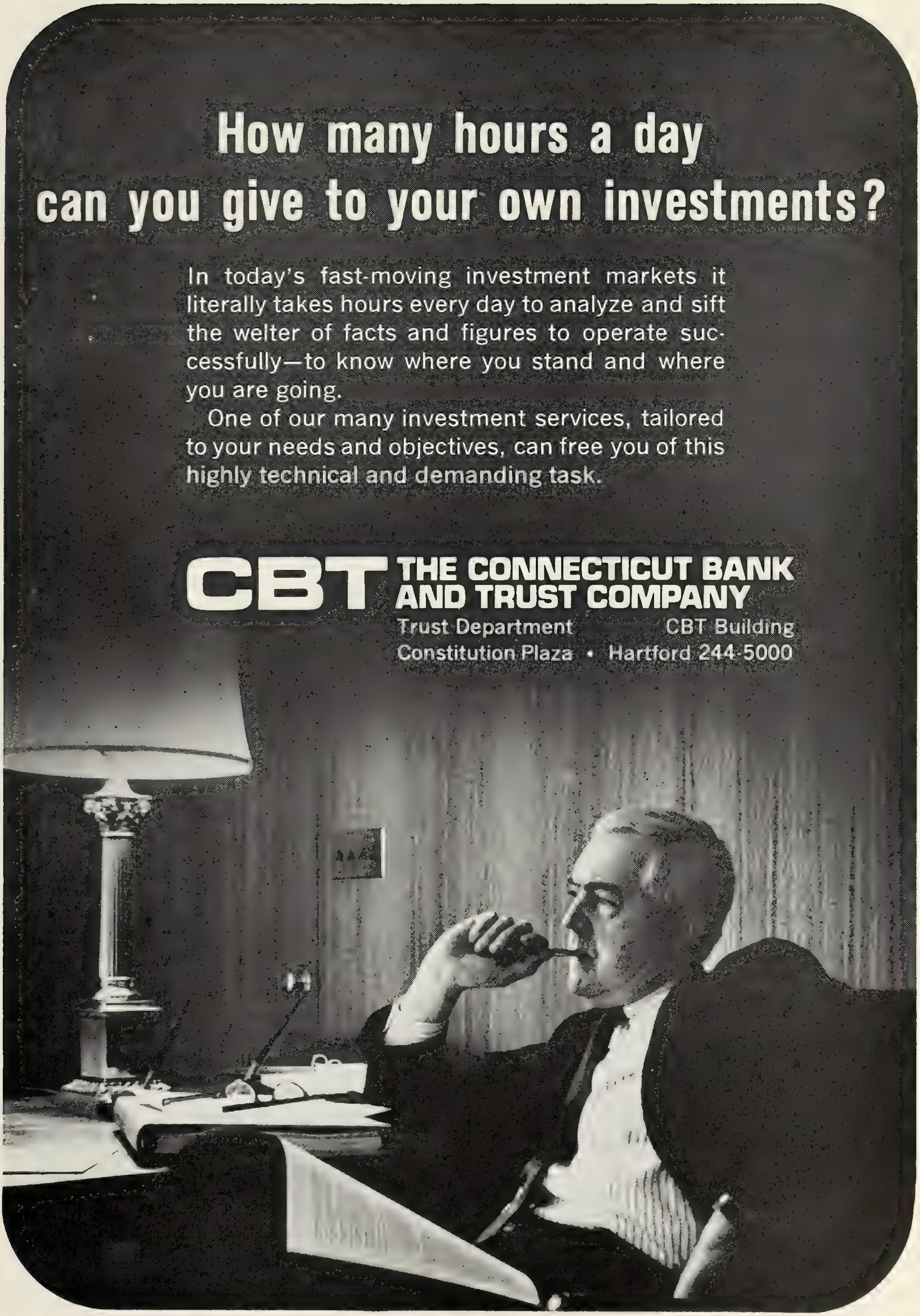
Physical Fitness And Cardiovascular Health

It is well recognized that oxygen transport and muscular system in trained subjects are qualitatively as well as quantitatively superior to those of untrained subjects. In the athlete a higher oxygen uptake is related to a greater capacity of the heart and lungs to deliver oxygen and of the muscles to utilize oxygen. There may also be an inborn limit to the anaerobic power that any individual can at-



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tain with training and Holmgren has suggested that a true index of physical fitness would be the actual power as a percentage of the potential power of an individual. But the fact is that we still lack a firm definition of fitness.

Ordinarily there occurs a 25 per cent decline in aerobic capacity between ages twenty and sixty.[1] Active participation in sports past the age forty delays this decline in aerobic capacity. This should be found in a study of the fitness of some of the primitive societies who require muscular work in order to survive. Theoretically the aerobic power of these people should be higher than that of modern societies. This was, in fact, found to be true by Lange Andersen[2] who found that the aerobic power of the Lapps from the northern Scandinavian peninusla was clearly higher than that of Oslo workers at all ages, particularly after age forty. The same is probably true of primitive men as against urbanized populations. Here again we have the complicating factor of fat found more abundantly in urbanized populations.

The main concern of cardiologists is whether there is any relationship between physical fitness and the frequency and morbidity of coronary heart disease (CHD). There is no available information on the relationship of maximum O_2 uptake or other measures of physical fitness to CHD rate. There is a lower incidence in the more active worker, but this may be due to other factors, than different levels of fitness, such as for example differences in personality, levels of occupational emotional stress, body build and composition, recreational habits and job selection by the more fit to perform physical work. It is highly probable that the subject more active in his work and play has a higher fitness level.

The cardiologist is concerned how to discriminate between the fit and unfit subject. It still remains to be shown that maximum O_2 uptake measurement is any better than some of the less sophisticated tests measuring a simple parameter such as recovery heart rate or the ballistocardiogram wave form in differentiating those who are likely to develop CHD from those who have some natural protection from CHD.

Investigators interested in the role of exercise in the prevention and treatment of CHD are as yet unable to provide conclusive answers. Exercise is not like a pill that is easily administered with little effort required on the part of the patient with a dose that may be accurately titrated against its effect on the patients blood. Even with a pill like an

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anticoagulant, coagulant therapy in CHD remains controversial.[3] Exercise cannot be put up in a capsule, the dose is difficult to gauge, a real effort is required on the part of the patient and the effects of the therapy are not easily measured. And so it is hardly necessary to apologize for the inability to provide exclusive answers to the value of physical fitness.

Future population surveys into the incidence of CHD hopefully will measure fitness with one of the available submaximal tests and will furnish answers to some important questions. Does physical fitness delay the development of CHD or prolong life? It is well known that muscular performance of the aged can be improved by physical conditioning. That this is also true of heart muscle is demonstrated by the changes in the BCG wave form and amplitude in the direction of those which characterize youth, which are found in older people after training. The BCG then should help to answer this question. Other questions such as optimal levels of fitness, what facets of fitness are desirable for health and longevity and how is this fitness best achieved are likely to have their answers in the years to come.

It is becoming popular to have patients who have recovered from acute myocardial infarction take part in physical exercise programs. These programs have definite merit in improving patient's morale and facilitating full rehabilitation. As patients who are recovering from myocardial infarction statistically speaking follow a predictable course, it should be possible to decide clearly over a period of five years whether these programs do anything for patients other than improve their well-being. To decide this important matter, however, a series of consecutive patients recovering from myocardial infarction would have to be referred to a rehabilitation center with one subject undergoing physical training while a matched control takes part in an equal number of sessions of non-athletic recreational programs.

It appears that the better the controls in past studies of CHD, the less the benefits can be shown to result from measures such as anticoagulant or anti-anginal agents. None of the exercise rehabilitation studies in CHD so far available for review have made any attempt to achieve the necessary levels of control. Discussion of the value or lack of value of physical fitness will go on for many years. Even if it will be shown that a high level of physical fitness reduces significantly the incidence and mortality of CHD, a major problem confronting public health officials will still be to motivate people to want fitness badly enough to do something about it.

Much work remains to be done but the Toronto Symposium[2] showed that physicians and physical educators and others in the health professions understand well the problems to be solved and methods needed to solve them. Hopefully they will work more closely in the future to work for health and longer life in quality as well as in quantity.

L.H.N.

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Tissue Immunity Against Cancer

Most physicians readily accept chemicals, viruses, irradiation and chromosome damage as oncogenic. It is, therefore, reasonable to expect immunologic defenses to protect against these influences. We know that not everyone subjected to these oncogenic agents develop clinical cancer. Why do some respond with cancer while others remain free? Is there an immunologic defense?

There are rare patients who undergo spontaneous regression of a malignant tumor and this documented fact has intrigued clinicians for decades. In 1950,[1] Dunphy made some observations on the natural behavior of cancer in man and described two patients who appeared to satisfy the criteria of spontaneous reversal of tumor growth. He raised the question of the role of active resistance of the host in providing variability of response encouraged by the statement of a foremost pathologist Ewing that "the lymphocyte is an important agent of defense against tumor growth."

This concept of tissue immunity against tumors has since become well established in experimental animals. For example in 1953, Foley[2] demonstrated that tumors induced by methylcholanthrene in animals produce antibodies which could induce resistance to a subsequent challenge. Gorer and O'Gorman[3] measured in vitro cytotoxicity in serum from tumor bearing animals. They showed that immunity to the tumor develops and this immunity can be transferred by syngeneic spleen cells from tumor bearing animals. Even RNA extracted from heterologous immune lymphocytes has been shown to induce regression of primary fibrosarcomas growing in rats.[4] There is little doubt then that experimental data support the concept that malignant cells are antigenically different from the host and, therefore, may be subject to immunologic attack.

The information about specific antigeins in human cancers is still meager. The presence of tumor specific antigens in human colon cancer was demonstrated by Gold and Freedman[5] in a series of experiments using the rabbit as the test animal. McKenna and his co-workers[6] have also identified a soluble specific antigen in 31 per cent of human cancers that was serologically identical with an antigen derived from HeLa cells. This type of experimentation was carried into the clinical field by Nadler and Moore.[8] They gave specific homologous "immune" leucocyte transfusions in the treatment of patients with melanoma and other malignant tumors. They reported seven patients as having objective responses to such treatment including two with a complete remission of almost two years.

To this type of immunologic information in the control of cancer must be added the experience of Wilson et al[7] who reported a case in which a metastatic carcinoma of the bronchus was inadvertently transferred to a thirty-four year old patient in renal failure via a kidney transplant. The metastatic focus in and around the transplanted kidney did not appear until eighteen months after the allograft was placed. The tumor did not respond to irradiation. Accordingly immunosuppressive therapy was stopped in the hope that the patient might retain the transplant and reject the tumor. Instead rapid rejection of the transplant occurred. The rejected transplant was removed but some nodes remained behind involved by metastatic epidermoid carcinoma.

During the next month the patient though febrile showed slow regression, the remaining tumor which finally disappeared and a biopsy of a node gave no further evidence of metastatic tumor. Six months after removal of the transplant, a complete groin dissection from the bifurcation of the aorta to the femoral triangle revealed no gross or microscopical cancer. Abdominal laparotomy also

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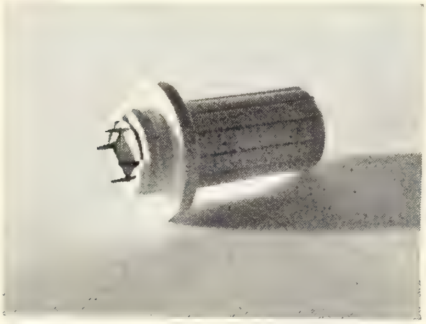

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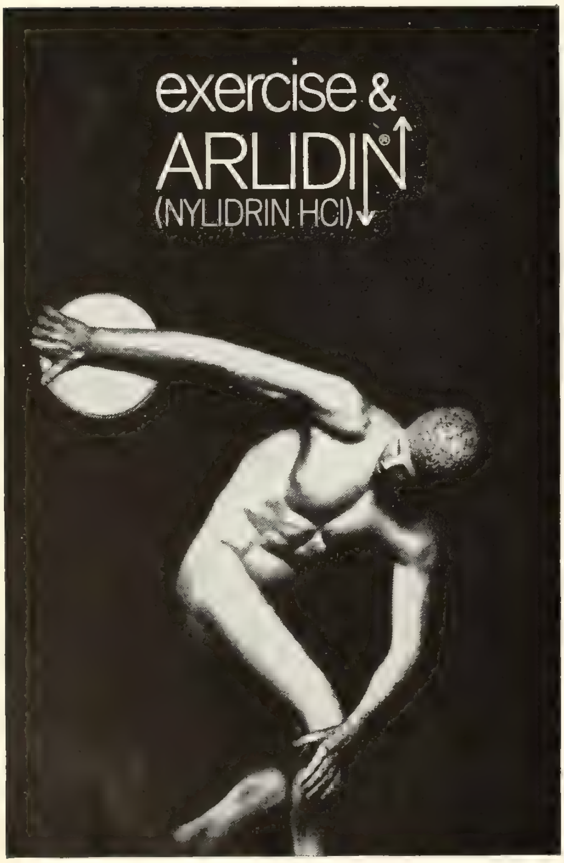

showed no tumor. The disappearance of residual tumor after immunosuppressive agents were withdrawn and nephrectomy performed accentuates the principle of immunosuppressive therapy for cancer.

Most attempts to increase the immune potential of the patient with cancer have hitherto been directed against his specific tumor rather than his general immune mechanisms. In Wilson's case the surgical procedures in themselves as well as irradiation and chemotherapy, all used quite generally in the treatment of cancer, actually impaired the patient's immune mechanism and only after immunosuppression was stopped did the patient recover his ability to reject the growing transplanted cancer.

Obviously defense mechanisms do exist in many subjects capable of protecting the magainst the ravages of malignancy. The challenge of the future is to learn how to manipulate these defense mechanisms in such a way as to prevent escalation to malignancy and to provide protection once clinical malignancy has been discovered.

L.H.N.

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Foreword

Dr. Adolph Magnus-Levy (1865-1955)

The demonstration by Dr. Magnus-Levy that metabolic rate was subnormal in myxedema and that the reverse was true in Basedow's or Grave's disease has been called the cornerstone of quantitative diagnostic methods in clinical endocrinology. The clinical significance of the thyroid in myxedema was recognized in the 70's but it was ignored in Grave's or Basedow's disease except by Moebius who hypothecated on clinical grounds that Basedow's disease was the counterpart of myxedema. That altered energy metabolism was a characteristic of thyroid disease was unsuspected. Magnus-Levy's demonstration that the metabolism was reduced as much as 50% in myxedema and increased as much as 50 to 100% in Basedow's disease confirmed Moebius' hypotheses. Dr. Magnus-Levy further showed that the metabolism of a patient with myxedema could be brought to normal in a month by feeding thyroid tablets and that it relapsed in 4 to 8 weeks after discontinuing the thyroid tablets. This was the first demonstration of naturally occurring diseases due to hyper-and hypo- functioning of the same endocrine gland.

Many fine studies of energy metabolism were done before Dr. Magnus-Levy's work. His first contribution was the concept of "grundumsatz" which Lusk and Dubois translated to basal metabolism. By utilizing measurement of metabolism for brief periods under standard conditions he was able to bring the measurements into clinical medicine. Within a few years he was able to complete his important studies in thyroid and other diseases. With his usual modesty Dr. Magnus-Levy, speaking to an assembly of friends in the twilight of his life, said "when working in the newly opened mines of metabolism, I never claimed to have found Old Gold but only to have succeeded perhaps in one or two Lucky Strikes."

Dr. Magnus-Levy made his mark as a distinguished investigator but he remained a compassionate physician. He was proud to have been a product and part of what he called "the heroic age of German medicine (1865-1914)". He attended lectures by Carl Ludwig and later studied under Bernhard Naunyn. He described the latter as the exponent of medical conscience in Germany, "for it is not only the discoveries and the kind of his teaching by which a scholar influences his pupils and his time but also and more so the scholarly and human standard set up by his life".

Alas those happy days in German medicine have vanished. Of his years in this country Dr. Magnus-Levy had this to say in a statement of thanks to be read at his bier:—

"To the land of the free which has accorded, among countless other exiles, to myself such generous reception, protection, and shelter and restored to all of us peace and dignity.

To the Medical Faculty of Yale University and especially Professor John F. Fulton who made it possible for me in the last minute to leave Germany. Thus in my advanced years come to me tranquility and ease and almost steady satisfaction such as I have never known before and had not expected to find in life".

Paul H. Lavietes, M.D.
Guest Editor

Correspondence between the late Dr. John F. Fulton and Dr. Magnus-Levy and his family was put at my disposal by Miss Madeline E. Stanton, Librarian of Historical Collections, Yale Medical Library.

The Clinical Use of Circulating Thyroid Autoantibodies in the Differential Diagnosis of Thyroid Disorders

Bruce F. Bower, M.D.

Introduction

The ability to detect and quantitate circulating antibodies against thyroid tissue has led to a considerable modification of the traditional concepts of thyroid disease.[1 2 3] At least four separate thyroid antigens have been identified and several techniques are available for demonstrating antibodies to each of these thyroid constituents. Recent simplifications have made certain of these determinations widely available at the clinical level where they have become important differential diagnostic procedures. Despite these facts most practicing physicians remain unaware of both the availability and utility of these procedures and continue to regard such studies as primarily investigative.

The results of over two hundred, consecutive, tanned sheep cell hemagglutination determinations performed in the Endocrine Unit Laboratory of the Hartford Hospital constitute the basis of this report. All sera examined were from subjects with known or suspected thyroid disease. The availability of commercially prepared stable reagents*, the inherent sensitivity and the technical simplicity of this procedure make it readily adaptable for use. The test is now routinely performed in the serology section of the Hartford Hospital and is performed by several commercial laboratories.** The clinical usefulness of this technique, not to the clinical investigator, but to the practicing physician and surgeon will be emphasized.

Methods

All patients were seen in consultation by one of the members of the Hartford Hospital Endocrine Clinic. Clinical diagnoses were established by conventional techniques employing standard laboratory assessment of thyroid function were indicated. Passive hemaggulatination titers with thyroglobuin-coated, tanned red cells were performed using a modification of the method of Boyden[4] employing control and thyroglobulin-coated sheep red cells[3]. Twofold serial dilutions of serum were routinely made from 1:10 to 1:2560 following absorbtion of serum with control cells to remove nonspecific hemagglutins. Additional dilutions were performed when indicated.

Results

The results of circulating thyroglobulin antibody determinations are presented in Table I and Illustration 1.

Normal Subjects: The upper limit of normal in this laboratory for the thyroglobulin antibody titer is 1:20. Our results are similar to others who have found approximately 6% of normal subjects

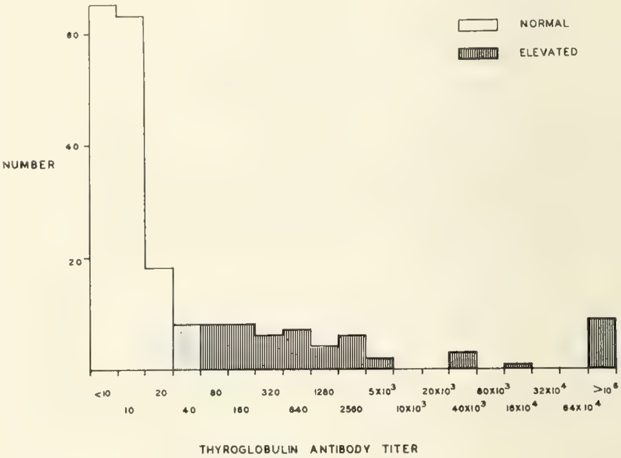

Figure 1

Distribution of Thyroglobulin Red Cell Hemaggultination Titers.

DIAGNOSIS

Distribution of Elevated Thyroglobulin Antibody Titers

Thyroglobulin Antibody Titer	Multi-nodular Nontoxic Goiter	Hashi-moto's Thy-roiditis	Idio-pathic Hypothy-roidism	Thy-rotoxi-cosis	Other
1:80-1:1250	12	5	6	7	0
1:2500-1:160,000	0	3	5	1	1
1:1,000,000	0	5	1	2	0

From the Endocrine Unit and Endocrine Clinic, Hartford Hospital.

DR. BRUCE F. BOWER, Clinical Endocrinologist, Hartford Hospital.

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have low grade thyroglobulin titers by similar techniques.[5 6] It is not clear why some apparently normal subjects have detectable thyroglobulin antibodies. This may represent thyroid injury of a nonspecific and subclinical nature, since such titers are seen with increasing frequency in older patients.

Titers of 1:40 on repeat determination were felt to be ambiguous and were not considered clearly abnormal. Seven patients (3%) had titers of this magnitude. Three of these patients were clinically abnormal. There was one case each of multinodular nontoxic goiter, thyrotoxicosis and a euthyroid sibling of a patient with established Hashimoto's thyroiditis and myxedema.

Discussion

As with all demonstrations of circulating autoantibodies, it is not clear whether thyroid antibodies cause thyroid destruction by antigen-antibody interaction or are present only as indicators of nonspecific destructive processes which disrupt normal tissue integrity. Thyroglobulin is considered to be a sequestered protein similar to sperm and lens protein and under normal circumstances it does not enter the circulation intact. As a result it is not recognized as "self" by immunologically competent cells if disruption of thyroid cells or acini allow intact thyroglobulin to enter the circulation[7]. Regardless of etiology, however, the presence of an elevated thyroglobulin antibody titer is of clinical relevance in several areas:

Hashimoto's Thyroiditis: Very high antibody titers occurred commonly in patients with clinical Hashimoto's or lymphocytic thyroiditis confirmed histologically[8]. The magnitude of the titer in many of these patients strongly suggests a primary initiating or sustaining role of these antibodies in an autodestructive, autoimmune thyroid process. Several patients, however, with normal thyroid antibody titers were found to have histiologic thyroiditis at operation. Hence, although a high titer (greater 1:2500) strongly suggests a diagnosis of Hashimoto's thyroiditis, a low or absent titer does not exclude the diagnosis.

The elevated titers in patients with clinical multindular nontoxic goiter and idiopathic hypothyroidism suggest that these superficially dissimilar disorders may be part of the spectrum of Hashimoto's thyroiditis. While the phenotype of multinodular goiter probably represents a heterogenous group of etiologic disorders, only some of which may be Hashimoto's thyroiditis, a compelling case has been made for considering idiopathic hypothyroidism as a late stage of autoimmune thyroiditis—the fibrous variant of Hashimoto's thyroiditis.[1 3 5]

It is important to obtain thyroglobulin antibody titers in the close relatives of patients with established Hashimoto's thyroiditis. Such patients are at increased risk of ultimate goiter, hypothyroidism or both and should be closely followed for such complications. An elevated titer may preceed overt evidence of thyroid dysfunction in such patients and early replacement with thyroid hormone is indicated.

An increasing number of patients with "adolescent goiter" are recognized as having Hashimoto's thyroiditis on the basis of elevated thyroid antibody titers[9]. This is a significant clinical distinction since thyroiditis and goiter, with or without hypothyroidism, is not a self-limited disorder and thyroid replacement therapy is indicated on an indefinite basis.

Subacute Thyroiditis: Elevated thyroglobulin titers were not seen in patients with subacute or de Quervain's thyroiditis in this series. In the present series only one of ten patients, with a clinical diagnosis of subacute thyroiditis, characterized by the abrupt onset of tenderness following a viral-like respiratory infection with a clinical response to steroid and thyroid therapy, had a significantly elevated thyroglobulin antibody titer. Thus it should be emphasized that "thyroiditis," per se, is not accompanied by significant elevations of the thyroglobulin antibody titer. The principal value of the titer in these patients is in the exclusion of the more chronic Hashimoto's thyroiditis.

Euthyroid patients on exogenous thyroid: The clinician is frequently presented with patients, commonly overweight young women, in whom thyroid therapy has been initiated on vague clinical grounds without adequate laboratory confirmation.

Previously it has been necessary to employ expensive and potentially hazardous thyrotrophin stimulation,[10] or to tediously withdraw therapy in order to identify patients in whom thyroid should be continued. Since the thyroglobulin antibody titer is not obscured by thyroid therapy[3], an elevated titer in such a patient indicates that the thyroid gland is damaged and that withdrawal of therapy will ultimately be accompanied by hypothyroidism, goiter, or both. In this series only one such patient with a normal antibody titer at the time of initial evaluation developed hypothyroidism following discontinuation of thyroid therapy.

In all other instances a normal titer correctly anticipated that replacement therapy could be discontinued. In patients with significantly positive titers, exogenous thyroid therapy was routinely continued.

Differential Diagnosis of Thyroid Malignancy: Many patients are subjected to unwarranted thyroidectomy as a result of an unexplained goiter or thyroid nodule in the absence of overt hypo-or hyperthyroidism. Frequently a pathologic diagnosis of thyroiditis is obtained. The finding of a significantly elevated thyroglobulin antibody titer (greater than 1:80) should suggest thyroiditis and dictate a trial of thyroid suppression prior to surgery. In many of the patients in this series a correct preoperative diagnosis could have been made and surgery possibly avoided had this sequence been followed. Several of the author's patients with elevated thyroglobulin titers, in whom such a trial was employed, had prompt remission of their thyroid "tumors". In at least one elderly patient with a titer in excess of 1:1,000,000 surgery was deferred despite many clinical features of infiltrative carcinoma of the thyroid. Subsequent clinical course confirmed the benignity of her disorder. It should be emphasized, however, that an elevated thyroid antibody titer does not exclude thyroid cancer. Several patients with lymphoma of the thyroid[3 11] and elevated antibody titers have been reported, and in one series 4 of 64 patients with carcinoma of the thyroid had titers in excess of 1:2500[3]. In contradistinction several patients with biopsy established thyroiditis had negative thyroglobulin titers. In this, as in all clinical judgements, the laboratory does not obviate a careful clinical assessment of the patient.

Thyrotoxicosis and thyroiditis: A surprising number of patients (10) with apparently uncomplicated Graves disease, with or without infiltrative ophthalmopathy, had elevated antibody titers. In several the titers were in excess of 1:1,000,000. The only clinically distinguishing characteristic of these patients was a positive family history of goiter or other thyroid abnormality in immediate family members.

This association, which has been referred to as "Hashitoxicosis," is recognized with increasing frequency now that thyroid antibody titers are more widely employed. It seems probable that at least some of the late hypothyroidism attributed to radioiodine or surgical therapy for thyrotoxicosis is a result of this frequently unrecognized, coexistent, autodestructive process. At the present time no patient in the endocrine clinic of the Hartford Hospital with a thyroglobulin titer of over 1:2500 is treated by either radioactive iodine or surgery without an initial trial of antithyroid drug therapy, since premature thyroid destructive therapy may hasten ultimate hypothyroidism. In at least three patients in the present series documented thyrotoxicosis has progressed to hypothyroidism during a two year period in which only propylthiouracil therapy was employed to control the hyperthyroid state.

Euthyroid exophthalmos: A not uncommon problem is presented by the patient with exophthalmos in the absence of clinical or laboratory evidence of hyperthyroidism[12]. This problem is compounded when the exophthalmos is unilateral, as it often may be in such patients, necessitating exclusion of a variety of retroorbital tumors and other mass lesions. The presence of an elevated thyroglobulin antibody titer indicates a coexistent thyroid abnormality and substantiates an endocrine etiology. In the present series three of five such patients were correctly identified on this basis. Subsequent studies of thyroid suppressibility and clinical response confirmed this initial impression. Again a single antibody determination was highly specific in establishing a correct diagnosis.

Differential Diagnosis of Primary and Secondary Hypothyroidism: Idiopathic primary hypothyroidism can mimic hypothyroidism secondary to pituitary insufficiency both clinically and by laboratory parameters since urinary steroid and gonadotrophin excretion may both be lowered by primary hypothyroidism. It is important to make this distinction since therapy of other trophic deficits is necessary in the secondary disorder. An elevated thyroglobulin antibody titer has been shown to constitute strong evidence for primary hypothyroidism. In the present series no patient with primary pituitary insufficiency and secondary hypothyroidism had a significantly elevated thyroglobulin antibody titer. Similar results have been reported by others in larger series of patients[13].

Summary

The thyroglobulin antibody titer as determined by the passive sheep cell hemagglutination technique is a simple and useful clinical tool in the differential diagnosis of thyroid disorders. It is not significantly modified by thyroid therapy. It provides unique amnestic information concerning past or present thyroid involvement by both specific

autoimmune and nonspecific thyroid disorders. It is of particular value in the assessment of the euthyroid patient on thyroid therapy, the patient with a potentially operative thyroid nodule or goiter and the patient with euthyroid endocrine exophthalmos. The simplicity of determination and clinical utility should make it a standard part of the laboratory evaluation of all such patients.

Acknowledgements

The author would like to thank the members of the Endocrine Clinic of the Hartford Hospital, and particularly Dr. Frederick Nichols for making their patients available for this study. Miss Arlene Royko provided excellent secretarial assistance.

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THE COURT OF LAST RESORT

It is no sign of ignorance or incompetency to fail to understand a case. To teach students that positive diagnosis can be made in all cases is an error. The rapid increase of means and appliances for ascertaining facts of disease and diseased conditions require more study and training and capacity for deductive reasoning. The older physician who makes a diagnosis often by mere intuition, may be quite as accurate as the younger man with a vast array of facts from instruments of precision. In one case we can follow and correct such reasoning, but in the other we cannot. Carlyle said mistakes and errors are inseparable from every human being, irrespective of all conditions. No field of thought requires more accurate perception and critical reasoning than that of medicine. The judge realizes that his opinion and the facts on which it is based will be reviewed by others, and it is a matter of personal pride to be correct. In a higher sense, the judgment of the physician should be sustained by the progress and history of the case. A court of last resort will finally pass on his judgment, beyond the selfish levels of pride and personality.—Two Mistakes, editorial, *JAMA* 19:235-236 (Aug. 20) 1892.

Primary Aldosteronism

Patrick J. Mulrow, M.D.

Introduction

Aldosterone is the predominant mineralocorticoid synthesized by the adrenal cortex. Healthy subjects eating a normal diet secrete 50-200 micrograms each day, but the amount of aldosterone secreted is increased by sodium depletion and decreased by sodium loading. Normally, there is a diurnal variation in the output of aldosterone resulting in a greater secretion rate during the day than at night. Activity and body posture are the major determinants of this diurnal rhythm.

Physiology

Regulation of Aldosterone Secretion

Unlike the other adrenal steroids, aldosterone is not under the direct control of the pituitary gland. Many physiological stimuli, such as sodium depletion, will increase aldosterone secretion in the absence of the pituitary gland. Although ACTH administration will initially stimulate aldosterone secretion, the secretion rate falls to or below control levels with continued administration. Clearly some other mechanism regulates aldosterone secretion. The pituitary gland, however, is important in maintaining the metabolic integrity of the adrenal cortex so that aldosterone secretion can respond maximally to a physiological stimulus.

The potassium ion also influences the secretion of aldosterone by a direct effect on the adrenal gland. Potassium loading increases, while potassium depletion decreases the secretion rate and can inhibit the stimulation by sodium depletion.

The major regulator of aldosterone secretion in man is the reninangiotensin system. Renin is an enzyme synthesized in the juxtaglomerular cells of the kidney (Fig. 1) and secreted into the blood, where it acts upon a protein in the alpha-2-globulin fraction to form a decapeptide, Angiotensin I. The decapeptide is rapidly converted to the octapeptide, Angiotensin II by a converting enzyme in plasma. It is Angiotensin II that is the active principle in this system. Besides being a potent pressor agent, it has direct effect on the adrenal gland to stimulate aldosterone secretion (Fig. 2). Indeed, it appears that the chief physiological role of the renin-angiotensin system is more as a regulator of aldosterone secretion than as a pressor substance.

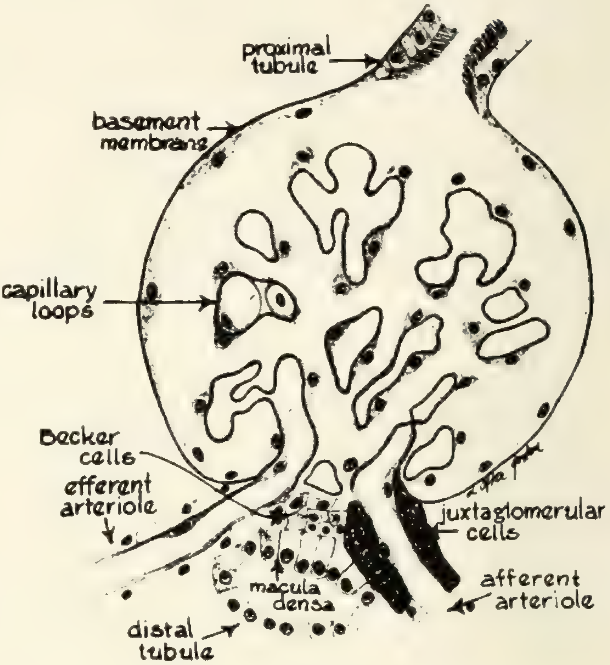

Figure 1
Diagram of Juxtaglomerular Complex

The mechanisms regulating renin secretion are not completely understood. The juxtaglomerular cells appear to act as baroreceptors. A reduction in renal arterial pressure increases while an elevation decreases renin secretion. It is thought that sodium loading and depletion influence renin secretion through changes in renal arterial pressure and volume, thus altering the stretch on the juxtaglomerular cells. An alternative hypothesis suggests

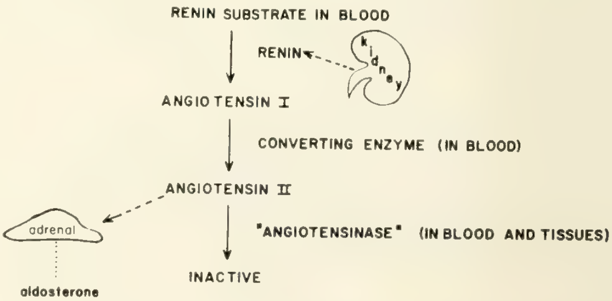

Figure 2
Diagram of Renin-Angiotensin System

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that it is the sodium concentration of the glomerular filtrate reaching the macula densa, the specialized cells of the distal tubule, which controls the release of renin.

Mechanism of Action

The major site of action of aldosterone is the kidney. Aldosterone enhances the reabsorption of sodium and the secretion of potassium by the distal tubule. The availability of sodium influences aldosterone's effect upon potassium secretion. In subjects on a reduced sodium intake, aldosterone does not cause a negative potassium balance. The potassium ion is secreted in exchange for sodium, and if less sodium is presented to the exchange site, less potassium will be secreted.

The sodium ion also determines the effect of aldosterone on blood pressure. Acute injections of aldosterone have no effect upon blood pressure but chronic administration of aldosterone to subjects on a high sodium intake will produce hypertension. A reduced sodium intake will prevent the development of hypertension. The exact mechanism of the hypertension is unknown. One hypothesis suggests that mineralocorticoids increase the water and electrolyte content of the wall of the arterioles with subsequent narrowing of the lumen and increased peripheral resistance[1].

In addition to its effects on the kidney, aldosterone alters the electrolyte composition of gastrointestinal, sweat and salivary gland secretions by decreasing the sodium and increasing the potassium concentration.

Clinical Syndrome of Primary Aldosteronism

The classical picture is one of a patient with benign hypertension and complaints of polyuria, polydipsia, nocturia, weakness, and intermittent paresthesias or paralysis. The physical examination reveals little other than benign hypertension; there is no edema. The laboratory findings characteristically consist of a dilute, neutral urine, a low serum potassium concentration and elevated serum bicarbonate and sodium concentrations. The BUN is usually normal. Carbohydrate tolerance is frequently impaired but overt diabetes is unusual. Most of the symptoms and laboratory findings, including the abnormal carbohydrate metabolism are due to potassium deficiency[2].

If aldosterone enhances sodium reabsorption, why do not patients with primary aldosteronism develop edema? It has now been clearly shown that the continuous administration of aldosterone to normal subjects does not produce edema. After a few days of sodium retention, the patient escapes from the sodium retaining effect of aldosterone but continues to lose potassium. Several recent reports indicate that a "factor" other than aldosterone failure of the escape mechanism is necessary for continuous sodium retention and the resulting edema formation.

The incidence of primary aldosteronism is a subject undergoing vigorous debate. Dr. Jerome Conn contends that a milder, more subtle form of the disease, normokalemic primary alodsteronism, is a common cause of hypertension. Because of the incidence of adrenal adenoma in autopsy studies of hypertensive patients, he has speculated that the incidence of primary aldosteronism may be 20% in the hypertensive population[3]. From his own series of hypertensive patients, he has found an incidence of 7% of normakalemic primary aldosteronism[4]. Two studies report the infrequent occurrence of excess aldosterone secretion in patients with benign hypertension[5, 6]. Nevertheless, it is clear that mild cases of primary aldosteronism with normal serum potassium concentrations do exist. Aldosterone excretion may also be in the normal range, although it may not respond to the stimuli which usually raise or lower it. Whether this kind of patient is a rare or frequent occurrence is not yet determined.

Diagnosis

An elevated aldosterone secretion rate with a low plasma renin level is diagnostic of primary aldosteronism. The plasma renin concentration is reduced because the excess aldosterone production leads to plasma volume expansion and inhibition of renin production. The juxtaglomerular cells "atrophy" and fail to respond to sodium depletion and the upright posture. Conceivably, a patient with primary aldosteronism who has been on diuretic therapy for an extended period may have a normal plasma renin concentration.

The usual plan of study is to discontinue all diuretic therapy, prescribe a normal to high sodium diet (150 to 250 mEq per day) for one to two weeks, measure serum potassium at frequent intervals, and aldosterone excretion or secretion rates toward the end of the period. Under ideal circumstances, careful potassium balance studies can be performed. The patient with primary aldosteronism will have a negative potassium balance, a fall in serum potassium and an elevated aldosterone production. In some patients, these abnormalities may be mild and barely outside the normal range.

The patient is then placed on a low sodium diet (10 to 20 mEq per day) and the plasma renin measured after 3 to 5 days on this diet. Plasma samples are usually collected in the morning while the patient is still supine in bed and after 4 hours of being up and about. In contrast to the normal subject, patients with primary aldosteronism have low to undetectable values. Aldosterone secretion also fails to increase in response to sodium depletion.

There are modifications of the diagnostic procedure but the principles are the same. Aldosterone secretion may be measured after 2 days of intravenous saline loading (2 liters 0.9% Na cl per day), and plasma renin may be assayed a few hours after the acute administration of a potent diuretic.

A less rigorous exclusion of primary aldosteronism may be obtained by several screening procedures. The patient is placed on a liberal salt diet for 2 weeks, and his serum potassium, blood pressure, and cardiac status are carefully monitored. If the serum potassium remains above 3.8 mEq per liter, primary aldosteronism is unlikely. A simple procedure is to infuse 2 liters of isotonic saline over 4 hours on two successive days. If potassium excretion is excessive, then primary aldosteronism is suspect[7]. This infusion test should not be performed in patients with severe hypertension, borderline cardiac status, or a serum K below 3.5 mEq per liter.

If the urinary potassium concentration is above 20 mEq per liter in the presence of a low serum potassium, or if the salivary sodium potassium ratio is 0.25 or less, then excess aldosterone secretion is probably present. All screening tests, however, should be viewed with caution.

Differential Diagnosis

The presence of hypokalemia in a hypertensive patient raises the suspicion of primary aldosteronism. Diuretic drugs are the most common cause of hypokalemia, and their effects may persist for a week or more after cessation of therapy. Gastrointestinal losses of potassium must also be considered; the chronic use of laxatives may be the cause.

Accelerated or malignant hypertension is frequently associated with secondary aldosteronism and hypokalemia. In this condition, the aldosteronism is due to the increased renin release from the severe vascular damage in the kidney. Primary aldosteronism can usually be excluded by the severity of the hypertension, especially the retinal findings, a low serum sodium and an elevated plasma renin concentration. Occasionally, these patients have renal artery stenosis. Correction of the arterial lesion will reverse the secondary aldosteronism.

Chronic pyelonephritis and other renal disorders with salt wasting may lead to secondary aldosteronism and hypokalemia. The BUN is usually elevated, the serum bicarbonate reduced and the renin levels elevated. Sodium repletion will correct the condition.

Cushing's syndrome occasionally presents with hypertension and hypokalemia and only mild signs of classical Cushing's syndrome. This is especially true of patients with non-endocrine tumors producing ACTH. The hypokalemia is due to the high cortisol production; aldosterone secretion is low.

Recently another syndrome with hypertension and increased aldosterone secretion has been described[8]. These patients appear to have a mild, congenital block in cortisol biosynthesis. The enzymatic site in the biosynthetic pathway that is deficient is not clear, but presumably the deficient cortisol production results in excess ACTH secretion. As a consequence, the increased precursor steroids are shunted into aldosterone production. Administration of a glucocorticoid such as dexamethasone corrects the hypertension and the hyperaldosteronism presumably by inhibiting ACTH secretion and the resulting excess aldosterone production.

There is also another congenital block in steroid biosynthesis (17-hydroxylase deficiency) which produces a syndrome mimicking primary aldosteronism and is due to excess desoxycorticosterone secretion. Aldosterone production is markedly reduced. Also, in the two cases reported, there is evidence of ovarian dystfunction from ovarian 17-hydroxylase deficiency. Again, exogenous glucocorticoids corrected the excess mineralocorticoid secretion, the hypertension and hypokalemia.

Treatment

The treatment of choice for primary aldosteronism is surgery. The adrenal tumors are quite small and rarely identified by retroperitoneal gas studies or aortograms. An intravenous pyelogram with nephrotomogram sufficies to rule out the rare case of adrenal carcinoma. The surgeon must be experienced in adrenal surgery. A pathologist familiar with adrenal pathology should also be present. Both adrenal glands must be exposed and the gland carefully dissected and examined for small nodules. Serial sectioning of the adrenal gland may be necessary to locate the small tumors. The tumors are usually single, occasionally multiple and bilateral, and rarely glomerulosa cell hyperplasia is all that is found. Unfortunately, bilateral adrenalectomy is sometimes necessary.

In preparation for surgery, the potassium depletion should be corrected by prescribing a low sodium diet, potassium supplements, and Aldactone. The serum potassium and BUN should be closely followed. The Aldactone should be stopped a few days before surgery. Postoperatively, the tendency to waste sodium and retain potassium because of the hypoaldosteronism can be managed easily by 1 to 2 liters of sodium chloride infusions for the first few days. The hypoaldosteronism may persist for several weeks but a liberal sodium intake is all that is necessary to prevent sodium depletion. The blood pressure may remain elevated for several weeks and occasionally months before returning to normal.

If surgery is inadvisable, then Aldactone and a low sodium diet will control the potassium wasting and the symptoms due to hypokalemia. Frequently the hypertension is also reduced. If it is not, standard antihypertensive therapy should be added and the medical theapy continued indefinitely.

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NINETEENTH CENTURY VIEWS ON THERAPEUTICS

The intrinsic tendency of a disease to recovery, or otherwise, is to be considered with reference to the value of therapeutical measures. Knowledge of the natural history of diseases is important as the true point of departure for therapeutics. Much has been acquired, within late years, in this branch of knowledge, but much yet remains to be acquired. Diseases which were formerly supposed to tend to a fatal result, if not treated by means of active remedies, are now known to end generally in recovery, if let alone. Examples are acute pleuritis and simple pneumonitis. The importance of increasing our knowledge of the natural history of diseases, by collecting cases which have pursued their course without active treatment, is to be kept in mind by those desirous of contributing to the advancement of therapeutics, and opportunities of accumulating such cases should not be neglected, always provided that the welfare of the patient be not compromised by withholding measures which we have good grounds for believing will be useful.

It may be laid down as a golden rule in therapeutics that active measures of treatment are only to be employed in cases in which they seem to the physician to be clearly indicated. The severity of disease, and the danger of the patient, be they ever so great, do not alone constitute grounds for the employment of active measures. If they are not useful, they will be likely to do harm. —Flint, quoted by Mettler, C.C.: *History of Medicine,* F. A. Mettler (ed), Philadelphia: Blakiston Co., 1947, p. 464.

Hyperthyroidism and Pregnancy

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When hyperthyroidism occurs in a pregnant patient, it becomes a more difficult disease both to diagnose and to treat. The "classical" clinical features of hyperthyroidism such as nervousness, heat intolerance, diaphoresis, goiter, and tachycardia occur in the euthyroid pregnant patient. In addition the parameters used in the laboratory diagnosis of hyperthyroidism are considerably altered in pregnancy. Finally, any therapeutic decision regarding the thyrotoxicosis must take into account the presence of a fetus.

Although it has been stated that conception rarely occurs in patients with untreated hyperthyroidism, and that in those cases where conception does occur there is an increased incidence of spontaneous abortion, there is little convincing evidence to support this contention. In fact pregnant patients appear to tolerate mild forms of hyperthyroidism well. Just as hyperthyroidism does not appear to make the pregnancy more difficult, neither does pregnancy appear to make the hyperthyroidism harder to control. It has been suggested that hyperthyroidism occurs more commonly in the pregnant than in the non-pregnant female. However, it is likely that this apparent increase is due to the fact that young women are rarely seen by physicians until they come to an obstetrician who makes the diagnosis.

In order to understand the difficulties in the diagnosis of hyperthyroidism in the pregnant patient, it is appropriate to review normal thyroid physiology during pregnancy. The BMR rises about 20% above non-pregnant levels but about 70-80% of this increase in oxygen consumption can be accounted for by the uterus and its contents, and the increased work of the maternal heart accounts for the rest. There is also a rise in protein-bound iodine (PBI) and butanol-extractable iodine (BEI) values to levels that are about twice normal (Table I). This elevation of the PBI determination has been found to be due to an increase in thyroxine-binding globulin capacity (TBG) due to increased estrogen production in pregnancy. TBG capacity increases from approximately 20 μg of T4 per 100 ml to 40 μg of T4 per 100 ml by the 12th week of pregnancy and remains at this plateau level. This increase in TBG also occurs in patients receiving the oral progestational agents and the diagnosis of thyroid disease may be equally difficult in this increasingly large group of patients. Since the red-cell or resin uptake of tri-iodothyronine (T3) from serum depends on the unsaturated binding capacity of TBG, the T3 test will also be altered in pregnancy. Although there is an increase in the amount of thyroxine bound to the TBG as evidenced by the elevated PBI, the increase in the binding capacity is greater still. As a consequence, uptake of I^{131} labelled tri-iodothyronine by the red-cell or resin (the T3 test) will be in the hypothyroid range. This combination of an elevated PBI value and hypothyroid T3 test is characteristic of pregnancy or estrogen therapy. The other major test of thyroid function, the uptake of I^{131} in the thyroid gland is elevated in pregnancy. However the fetal thyroid gland concentrates I^{131} by about the 12th week of gestation and because of the danger of radiation injury to the fetus, this test would be contraindicated in pregnancy even if it were useful. Although the above observations suggest that thyroid function is increased during pregnancy, the free thyroxine level which is thought to represent the metabolically active thyroid fraction is not elevated in normal pregnancy, and the available evidence indicates that thyroid function is not increased during normal pregnancy.

Table I

Normal Values for Thyroid Function Tests in Pregnancy

Determination	Pregnant Normal	Non-Pregnant Normal
PBI	6.5-11.5 μg%	4.0-7.5 μg%
BEI	5.5-10.5 μg%	3.2-6.5 μg%
T_3-RBC Uptake	10%	11-17%
T_3-Resin Uptake	10%	25-30%
Free Thyroxine	1.4-2.5 m μg%	1.4-2.5 m μg%

The presence of the eye signs of Graves' disease, a rapid resting pulse, tremor, and weight loss, or less than the usual weight gain are suggestive of hyperthyroidism in the presence of pregnancy. A PBI value above 12 μg per 100 ml, especially in conjunction with a T3 test in the normal range, is helpful in making the diagnosis. Determinations

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of unbound or "free" thyroxine are becoming available clinically and may provide useful information in this situation.

The major therapeutic choice in pregnant patients with thyrotoxicosis lies between surgery and use of the thiourea derivatives. The choice of therapy is often made according to whether the patient is referred to a surgeon or an internist, but either choice poses difficulties. Bell and Hall reported a series of 42 patients who underwent subtotal thyroidectomy for hyperthyroidism during pregnancy[1]. In the first 21 patients, there was a fetal loss of 24% but the second group of 21 patients were given desiccated thyroid post-operatively, and there was only one instance of fetal loss. The authors concluded that it was of the utmost importance to prevent hypothyroidism in the mother and suggested that patients routinely be given thyroid hormone post-operatively.

Hawe reported a series of 33 patients on whom subtotal thyroidectomy was performed with only one fetal loss, while in 3 pregnancies treated medically there were four abortions, two instances of thyroid crisis, and two cases of thyro-cardiac failure[2]. The data would appear to indicate that surgery is the treatment of choice, but there is a definite bias in this type of study. All the patients were prepared for surgery with antithyroid medication. Furthermore, operation was usually deferred until after the first trimester to avoid the period of greatest liability to abortion. As a result any patient who aborted during the first trimester was almost by definition a medical failure. In fact two of the patients who aborted while receiving antithyroid medication were being prepared for surgery. Similarly, the patients who were in cardiac failure or thyroid crisis were not considered operative candidates.

Although good results have been obtained after subtotal thyroidectomy, surgery is not an ideal treatment. In addition to the added risk in pregnancy of fetal anoxia, there is a certain mortality rate to any operative procedure, and significant complications occur such as hypoparathyroidism and laryngeal nerve paralysis which are difficult to treat. If a subtotal thyroidectomy is to be performed, it should be done after the first trimester when the pregnancy is most stable. The hyperthyroidism should be brought under control prior to surgery. This can be done with propylthiouracil (PTU) 100 mg every eight hours until the patient is under control which may take 3-4 weeks. Two weeks prior to surgery five drops of Lugol's solution twice a day should be added to the therapeutic regimen in order to decrease the vascularity of the gland. Iodides in big doses may cause fetal goiters which may become large enough to cause obstructive symptoms. It is worth noting that saturated solution of potassium iodide (SSKI) is six times as potent as Lugol's solution and the two should not be used interchangeably. Following surgery, the patient should be maintained on desiccated thyroid 180 mg a day for the rest of the pregnancy to prevent the possible complications of hypothyroidism. After delivery the thyroid hormone should be withdrawn and the patient's thyroid status evaluated.

In this country the medical treatment of thyrotoxicosis is mainly based on the use of thiouracil derivatives—propylthiouracil or methimazole (Tapazole). Thiourea drugs cross the placenta readily while thyroid stimulating hormone (TSH) apparently does not cross the placental barrier, and thyroxine does so only poorly. As a consequence fetal thyroid function may be inhibited by the anti-thyroid medication, while fetal TSH production stimulates the gland to compensate for this inhibition. After a period of time, a goiter may develop. If sufficient maternal thyroid hormone crosses the placental barrier, fetal TSH production will be inhibited and no goiter will occur. This interrelationship between the thiourea drugs, thyroid hormone, and TSH probably determines whether or not a goiter will occur in the fetus.

While TSH does not cross the placental barrier, long-acting thyroid stimulator (LATS) which has been implicated in the etiology of Graves' disease does. There have now been several reports of neonatal thyrotoxicosis occurring in infants whose mothers had Graves' disease[3]. Both mother and child have had a positive LATS assay which eventually became negative in the infant in association with a spontaneous regression of the thyrotoxicosis. For reasons that are not clear neonatal thyrotoxicosis occurs rarely although about 50% of patients with Graves' disease have a positive assay for LATS.

Astwood was the first to report a series of 19 patients who were treated with thiourea drugs during 22 pregnancies[4]. When the patients became euthyroid, the amount of PTU was decreased to 50 mg every eight hours, and in most instances, smaller doses were given during the last half of gestation. With this regimen all 22 children were born alive and well without goiter.

Becker and Sudduth treated 20 patients with anti-thyroid drugs and noted three abortions and two still births[5]. Three of the offspring had goiters. One goiter was large enough to cause death and one occurred in a cretin. The large goiter occurred in a mother who was also receiving large doses of iodide. It is not clear exactly how these patients were treated, but the authors felt that subtotal thyroidectomy was the treatment of choice.

Herbst and Selenkow reported 32 pregnancies occurring in 24 thyrotoxic patients who were treated with PTU in doses of 200-300 mg a day[6]. Once there was an amelioration of the signs and symptoms of hyperthyroidism, two or three grains of desiccated thyroid hormone were added even if the dose of PTU could not be reduced further. Twenty-nine pregnancies resulted in healthy new born infants, four of whom were premature. There were three pregnancy losses, including an abortion, still birth, and neonatal death for a total pregnancy loss of 9.4 per cent. No instances of neonatal goiter were found but recognition of these goiters may be very difficult, and they are often found only after a low PBI value is obtained.

The rationale for combining thyroid hormone replacement with anti-thyroid drugs is that it may protect the mother and fetus against the deleterious effects of hypothyroidism. This therapy will undoubtedly prevent maternal hypothyroidism, but whether it will prevent neonatal goiter is less clear. Thyroid hormone crosses the placental barrier poorly, and whether three grains of desiccated thyroid given to the mother will effect the level of thyroid hormone in the fetus has yet to be demonstrated.

In a retrospective study at this hospital of 41 pregnancies in 30 patients who received anti-thyroid medication during pregnancy, there were five instances of fetal death, and five of the pregnancies resulted in infants with neonatal goiter[7]. The dosage of PTU appeared to be important in the development of goiter in the offspring but was probably not the only factor. Although neonatal goiter did not occur unless the mother was taking more than 100 mg of PTU a day, one patient who was receiving 800 mg of PTU at the time of conception, and who had received 450 mg PTU a day throughout pregnancy did not bear a goitrous child. Maternal hypothyroidism, degree of control of the hyperthyroidism, iodide therapy, and a family history of thyroid disease also did not appear to be the major determinants of neonatal goiter.

In two instances where the data was available, the goitrous child had a BEI determination in the hypothyroid range while a simultaneous maternal determination was in the normal range for pregnancy. This finding would suggest that the difficulty in correcting a fetal PBI depressed by PTU does not lie with the amount of maternal thyroid hormone available but rather with an inability of this thyroid hormone to pass the placental barrier.

Since the goiters are usually not harmful in themselves, the major concern is whether there is an adverse effect on subsequent growth and development. This in turn is part of the larger question as to whether PTU therapy in the pregnant patient has any harmful effects on the subsequent development of the offspring. Fifteen children from the previously reported study[7] were available and were compared to 18 siblings who had not been exposed to PTU. History and physical examination, laboratory determinations, and psychological testing were done on these children. Although the small size of the sample made definite conclusions unwarranted, the data did not suggest that PTU therapy during pregnancy had an adverse effect on subsequent growth and development.

A reasonable approach to the therapy of hyperthyroidism in pregnancy would be to treat with PTU 100 mg every eight hours. Once control has been achieved, usually within a month, the dose of PTU should be lowered to 50 mg every eight hours. If the thyrotoxicosis is still controlled, the PTU should be lowered further to 75-100 mg PTU a day. Desiccated thyroid hormone would not be added to the therapeutic regimen unless the patient became hypothyroid. Since pregnant patients do not tolerate hypothyroidism well but do seem to tolerate hyperthyroidism, it is preferable to under-treat rather than over-treat the patient. If the patient has been reasonably controlled, the chances of "thyroid storm" occurring are remote. If the patient does become hypothyroid, she should be treated with 180 mg of desiccated thyroid; any less would probably not be sufficient in pregnancy. A cord blood should be obtained at the time of delivery for a PBI determination. If this is low, then the child should be treated with desiccated thyroid.

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CONVERSING WITH THE PATIENT AND HIS FRIENDS

To patient or to patient's friend simple and unmistakable language should be used; veiled statements are too apt to be misinterpreted. The words must be chosen thoughtfully. The word "disease" should never be used; disease of the heart conveys at once to most patients the idea of something incurable and threatening. The language should be as untechnical as it can be made. A patient has a right to be told what ails him, if he so desires, in terms that convey an idea of the magnitude and significance of the trouble; he has no right to technical diagnostic terms, and it is very rarely wise to parade these before him. Accurate information cannot be conveyed by means of strange words, which to unaccustomed ears bring unintended meanings; and for many the word once caught up becomes a matter requiring search in medical books, or a topic of debate with other patients. Thus the word "angina" should never come first from a doctor, if it is understood at all it will convey in almost all instances an ominous meaning; yet the prognosis varies up to fifteen years. The word "dropsy" is to be avoided, and the adjective "malignant" eliminated completely from the medical man's vocabulary. The valves should not be named, nor murmurs mentioned. These names and details should be of no concern to patients. Methods of examination likewise require little or no explanation; a clear example of the unhappy effects of unnecessarily disclosing technical detail is the well-known instance of high blood-pressure readings.—SIR THOMAS LEWIS (*Diseases of the Heart* Macmillan Co. Ltd.) .*The Quiet Art: A Doctor's Anthology.* Compiled by DR. ROBERT COOPE, Edinburgh & London, E. & S. Livingstone Ltd., 1952, p. 237.

The Management of Juvenile Diabetes Mellitus in the Post-Acidotic Stage

Jerome A. Grunt, M.D., Ph.D., and Paul S. Goldstein, M.D.

Although it is usually estimated that patients with juvenile diabetes mellitus make up about 5% of the total number of diabetics, there is a wide spread clinical impression that the rate of increase of new juvenile diabetics has been greater than the rate of population growth over the last 5 years. In addition, with the advent of insulin, the life span of the juvenile diabetic has increased to more than three-quarters that of normal. In light of the current shortage of physicians, these two factors make it very likely that more and more physicians will be faced with the management of patients with juvenile diabetes.

The clinical course of diabetes in young people is very different from that of mature onset diabetes. This stems in part from the consistently changing metabolism of growing children, but also from the fact that children with this disease are almost 100% insulin dependent. Autopsy findings and serum insulin studies have substantiated the complete lack of pancreatic islet tissue and endogenous insulin after 3-4 years of disease.[1]

In addition to growth and insulin dependence, other factors contributing to the extreme variability in the day-to-day course of the juvenile diabetics are the more frequent infections of childhood, increased and more fluctuant activities, more irregular eating habits, and finally, and most importantly, a labile, immature emotional fabric. These difficulties often tax the patience of the physician and lead to inadequate management.

Management of diabetes at the Yale Pediatric Endocrine Clinic is based on the following criteria of good control: 1. The relief of all symptoms i.e., polyuria, polydipsia, ketonuria, and the prevention of hypoglycemia; 2. The maintenance of growth and nutritional status to the optimum constitutional potential of the child; 3. The development of the patient's independence in the handling of his or her disease; 4. The development of an emotional state that is compatible with a full, productive, happy life. This approach can be applied to private practice with ease.

It is desirable to hospitalize all patients initially when the diagnosis is highly suspect or known. This allows for the re-establishment of nutritional, fluid and electrolyte homeostasis, as well as the determination of an initial insulin requirement. Even more importantly, the hospitalization is used to begin the long term education of the patient and his parents.

The essential pathophysiology is explained as is each procedure to allow an ever increasing knowledge of the disease process and its management. If the child is 7 years of age or older, an attempt is made to have him take responsibility for his own care. This includes: learning to administer his own subcutaneous injections; testing for urinary sugar and acetone and charting results. It also includes, learning to maintain general stability in relationship to diet, activity, and insulin dosage. It is important that these aspects of diabetic control become a way of life prior to the onset of adolescence. Patients who do not take the responsibility for their disease by 12 years of age often fail to achieve independence (from their parents re: injections, urine tests, emotional stability, etc.) until 16 or 17 years of age.

The attitude of the physician to the family unit at the beginning of management cannot be over emphasized. An optimistic outlook providing for minimal disruption in the usual day-to-day activities of the whole family provides an educational and emotional foundation which is rewarding during the ensuing 10-15 years.

Once ketoacidosis has been controlled, several needs of patient care must be met. These include: determination of the type and amount of insulin needed; determination of the renal threshold for glucose; and, the initiation of an educational program.

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Insulin

In studies recently undertaken in the Yale Pediatric Endocrine Clinic, we have demonstrated that there are different patterns of glycosuria in different children. In some children the heaviest glycosuria occurs during the day, in others during the night and in still others fairly evenly throughout the 24 hours of the day. These patterns do not seem to be related to the duration of the disease. Because of these findings, the choice of insulin must be individualized. All of our patients are discharged on one injection of insulin prior to breakfast.

During the period of ketoacidosis, following re covery from the immediate crisis, crystalline insulin is administered every 4 hours depending upon the degree of urinary sugar and acetone spillage. (All patients over 4 years of age are given insulin in the following manner: for a 3 plus sugar 12 units of regular insulin are given if no acetone is present and 15 units if there is acetonuria; when there is a 4 plus glycosuria, 16 units of regular insulin are used if the urine is acetone free, and 20 units if acetone is present*.) Although this approach requires that the patient be carefully observed, especially during those times when the blood sugar would be expected to be lowest, it usually shortens the length of hospitalization by several days. Patients under 4 years of age are often extremely insulin-sensitive. Small doses of insulin often convert a state of ketoacidosis to one of hypoglycemic shock. Great care must be exercised in using insulin in these children and the sliding scale should be based on 1-2 units of regular insulin for each plus of urinary sugar. The initial single morning dose of long-acting insulin is then taken as 50 to 75% of the total amount of regular insulin needed to maintain an acetone free urine and a moderate glycosuria in the few days following the control of ketoacidosis. The dose is then adjusted depending on the degree of glycosuria and the pattern of the urinary spillage. In those patients whose glycosuria is predominantly a daytime occurrence, NPH insulin alone or NPH with regular insulin suffices. However, if glycosuria is a predominantly nocturnal occurrence or spread equally throughout the 24 hours, Lente insulin or a mixture of Ultra and Semi-Lente insulins are more appropriate. We do not use PZI in treating children because of the possibility of unrecognized hypoglycemia during the hours of sleep and because of the manner with which PZI and regular insulin combine.

Renal Threshold and Urinary Sugar

Since blood sugar is rarely determined once the patient leaves the hospital, it is most important to relate the blood sugar to the urinary sugar several times during the hospitalization. If there is no renal disease, the single "second voided" urinary sugar (we ask our patients to carry out urinary sugar testing on a urine specimen obtained 10-20 minutes after an initial voiding) is as adequate as a single blood sugar for the control of diabetes. Although our patients report their daily pre-meal urinary sugars, we rely heavily on fractional 24 hour urinary sugar determinations in order to control this disease. Such determinations are made on each visit. Total urinary sugar is determined on four specimens: 8:00 A.M. to 12:00 noon; 12:00 noon to 4:00 P.M.; 4:00 P.M. to 8:00 P.M.; 8:00 P.M. to 8:00 A.M. The single morning injection of insulin is changed accordingly: regular or semi-Lente insulins to control the 8:00 A.M. to 12:00 noon sugar loss; NPH or Lente insulins for the afternoon and early evening urinary sugar spillage; and, Ultra-Lente insulin for the overnight urinary losses. This allows for a more rational approach to control the diabetes than does the blood sugar, since blood sugar may vary so from day to day and from time to time in the same day.

Some clinics define "diabetic control" as that condition in which there is a urinary loss of no more than 5 to 10% of ingested carbohydrates per 24 hours.[2] From our experience to date, we would seriously question whether the loss of an additional 10 to 25 grams of urinary sugar is of any consequence if the above stated goals for good management are met. Much has been written about basing diabetic control upon degrees of glycosuria. This approach has held that hyperglycemia and glycosuria are the primary factors contributing to the so called "complications" of diabetes. However, after an extensive review of the world literature, Dr. Harvey Knowles verified the impression that there is little if any correlation between vascular complications, dietary control and glycosuria.[3] By using urinary sugars we have found that we are able to achieve good control without the use of blood sugar determination. Thus, our patients face their visits to the doctor's office without fear of venipuncture.

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* We use Clinitest Tables for routine urine testing. Of great significance are the comments published by the Ames Company on the interpretation of this test. "Careful observation of the solution in the test tube while reaction take place and during the 15 second waiting period is necessary to detect rapid 'pass-through' color changes caused by amounts of sugar over 2%. Should the color rapidly 'pass-through' green, tan and orange to a dark greenish-brown, record as over 2% sugar with comparing final color development with the color chart".

Education

In addition to the treatment of severe ketoacidosis, the justification for hospitalization in most patients is the need for education, since few juvenile diabetics now come to the hospital in severe ketoacidosis. The responsible physicians should take the time required to discuss this disease fully with the children as well as their parents. Early in the treatment we give our patients and their parents a brochure on diabetes.[4] This offers them a chance to think about the printed words along with the initial statements of the physician. Once they have read the booklet, we again discuss their questions, fears and uncertainties. Many such sessions are required. This type of ongoing education should be continued at each subsequent visit once the patient has left the hospital.

A major role in the educational process of the hospitalized child and his family is carried out by the nursing staff. Both the patient and his family must be taught the following: how to sterilize the syringe (although many patients often use disposable equipment); how to inject insulin; how to test for urinary sugar and acetone; and, how to record daily urine test results. In addition, the nursing staff should be knowledgeable enough to be able to answer appropriate questions about diabetes in relationship to the skills they teach.

During the patient's hospitalization, the family consults with the dietician. This is done primarily to acquaint them with a normal diet for any child at a given age; and with the use of our exchange sheets which are based on those of the American Diabetic Association but modified to include foods often eaten during childhood. Our goal is to provide three well-balanced meals supplemented by two or three mid-meal snacks depending on the age and school status of the child. There is no diabetic diet prescribed, however, the diet should take national origin into account and an effort is made to avoid wide carbohydrate swings and to concentrate on higher protein-containing foods. The extremes of dietary involvement are avoided. The diet is not "free" and the foods are not weighed. No attempt is made to bend the child to the diet; rather, the diet is bent to the needs of the child.

One of the major hurdles to be overcome is that of the child giving himself his own injection. A critical point is reached in the instruction where the only remaining stumbling block is the psychological one of plunging the filled syringe into the skin. We have found that this is easily accomplished by having a "shot" party preferably with mother, father, child and physician or nurse involved. All present practice giving injections of normal saline in disposable syringes to one another. The family quickly learns that with the use of disposable needles little pain is produced. After injecting another person a few times, the patient usually can inject himself.

It is important for everyone involved with the patient during hospitalization to realize that he is not having his disease regulated for hospital living but rather for normal activity at home. Two logical steps follow this type of reasoning: 1) the patient must be kept quite active while in the hospital (total inactivity while hospitalized will make regulation for the patient's normal needs far more difficult); 2) the patient need *not* have his disease regulated tightly prior to being discharged. Almost all patients need less insulin once they are carrying out normal activities at home. In addition, the total requirement usually decreases over the initial few weeks following the onset of therapy.

Many new anxieties become evident when the patient is discharged. Both the patient and his parents are usually very anxious about assuming new responsibilities at home. This anxiety is decreased by a routine which the physician should use in order to help establish a feeling of independence. For the first week, the child or parent calls the physician every morning to check on insulin dosage. During the second week, the call is made every other day, then every third day, and finally, at prolonged intervals. This approach has been very helpful to all concerned and allows for a smooth transition from institution to home. The child is seen in two weeks, then a month, then every three months. During these times, the continuing education is of great importance! Several factors should be discussed frequently during these periods of ongoing education.

1. The need for assuming responsibility and the development of independence on the part of the patient are stressed.
2. The importance of having teachers and friends made aware of the patient's diabetes is discussed. There need be no shame associated with this disease.

3. The span of action of the type of insulin being used is reviewed frequently with the use of graphs.
4. Much time is spent discussing the approach to changing insulin dosage. Such changes should depend on the previous 3 to 7 day's pattern of glycosuria. Adjustments are not made on the basis of single tests or even on the previous day's tests unless there is acetonuria, marked polyuria or hypoglycemia. When changes are necessary, these are usually made in steps of 10 percent of the total dosage. Changes in insulin dosage also depend on the results of the quantitative urinary sugar findings. These changes are carried out by the physician as outlined above.
5. An approach to illness is outlined. Patients whose disease is of recent origin should contact their physician when they have an infection or when they are stressed. Although many patients need additional insulin at such times, this need should be individualized. Eventually, the patient is knowledgeable enough to be able to increase his insulin dosage himself. Vomiting accompanies many childhood infections and often leads to hospitalization. The patient and his family should be versed in the use of anti-emetics and frequent small amounts of iced sugar-containing clear fluids. If vomiting becomes intractable, there should be no procrastination to the use of a short course of intravenous fluids in the office or emergency room.
6. Patients are taught what to do in an emergency. Sweetened juices and glucagon are used in case of hypoglycemia and, either crystalline or semi-lente insulin in case of ketoacidosis.

It is important to keep in mind that children with diabetes mellitus need a doctor who is able to relate to them and in turn, have them relate to him. If the patient denies his disease and as consequence is rejected by his doctor, this is often the first of many subsequent serious problems. A physician who can give guidance and care, and who has the patience and time to help the young diabetic work out his problems, will provide the independent emotional basis that is is necessary to establish an adolescent period free from disaster.

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I learned in the regiment and in the class of conclusion at least of what I think the best service that we can do for our country and ourselves. To see so far as one may and to feel the great forces that are behind every detail . . . to hammer out as compact and solid a piece of work as one can try to make it first rate, and to leave it unadvertised.—Justice Oliver Wendell Holmes. Class day exercises on the 50th anniversary of the Harvard Class of 1851, June 28, 1911.

Myxedema and Hemorrhagic Pericardial Tamponade

Louis J. Elsas, M.D.

The "myxedema heart" was proposed as a clinical entity to include cardiac enlargement, sluggish cardiac action, and specific electrocardiographic changes which revert to normal with thyroid therapy[1]. The cause of cardiac enlargement remains uncertain and has been attributed, at least in part, to an associated pericardial effusion rather than to dilatation or hypertrophy of the heart alone[2]. In hypothyroidism, pericardial effusions of considerable size have been aspirated during life[3] and at autopsy[4], but tamponade remains extremely rare.[5] [6]

This communication records a case of myxedema which presented as hemorrhagic pericardial tamponade, a finding which to my knowledge has been recorded only once before in the literature[7]. The response of the pericardial effusion to pericardiocentesis and to thyroid replacement therapy is discussed and related to the response of other parameters of myxedema. A mechanism for the pathogensis of hemorrhagic pericardial tamponade is postulated.

Case Report: A 37 year old negro father of four was admitted to the Yale-New Haven Hospital complaining of shortness of breath and weakness. Over the previous ten years the patient noticed a puffy face and a preference for warm weather, intermittent exertional fatigue and dyspnea. However he continued to work daily as a self-employed trucker, moving furniture and other heavy objects. Two months before admission he fell "spread eagle" from his truck onto his back. Although he suffered immediate shortness of breath, his symptoms were transient, and he returned to his daily chores. Four days before admission he noted the onset of progressive muscle weakness, increased abdominal and facial bloating, exertional dyspnea, nocturnal orthopnea, eructations, and a sensation of "coldness". On the night of admission he became severely, weak, faint, and short of breath in the sitting position.

On examination he was in acute respiratory distress, belching, and disoriented to time. The blood pressure in both arms was 100/60 mm Hg; pulse was 70/minute; respirations 22/minute; and oral temperature 97 F. A weak, thready radial pulse disappeared on deep inspiration and on valsalva maneuver. The skin was pallid, yellow tinted, cool, and dry. There were xanthelesma over the upper eyelids, and brawny edema around the eyes and lips. Cerumen was present in the external auditory canals. The thyroid was not palpable. No heart sounds were audible and no precordial pulsation was palpable, although there was dullness to percussion across the entire precordium. Jugular veins were distended and filled from below. There was dullness to percussion to the subscapular areas over both lung fields. The liver was tender and palpable three finger breadths below the right costal margin. The patient had memory loss and was disoriented to time. His muscles were prominent, but weak, slow moving, and myotonic. Deep tendon reflexes were sluggish and pendular.

A radiograph of the chest demonstrated an enormous heart (Fig. 1) and an angiocardiogram (Fig. 2) confirmed that a massive pericardial effusion was present, but that cardiac chambers were of normal size. Reflux of dye into both azygos and hemiazygos veins, and a right atrial pressure of 250 mm of saline confirmed the presence of pericardial tamponade, with right heart failure. Accordingly, pericardiocentesis was performed, and thirteen hundred milliliters of viscous, brown-green fluid was aspirated and 150 ml of air was placed in the pericardial sac (Fig. 3). An estimated three liters of fluid remained in the pericardial

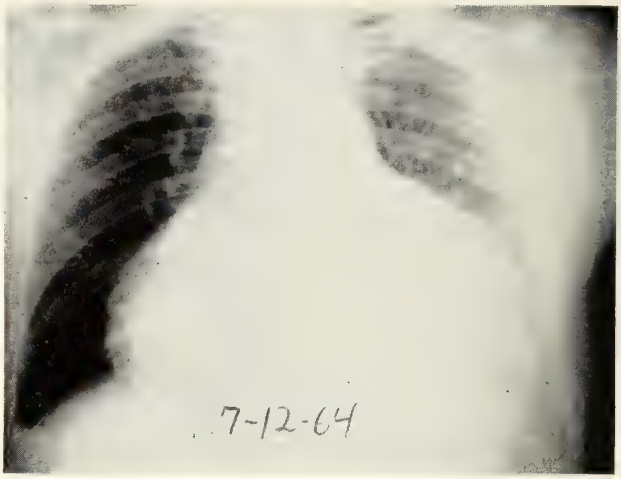

Figure 1
Radiograph of chest (PA) taken on admission showing an enormous heart shadow with bilateral pleural effusions.

Supported by a Special Postdoctoral Fellowship 1-53-Am-35, 615 of the United States Public Health Service.

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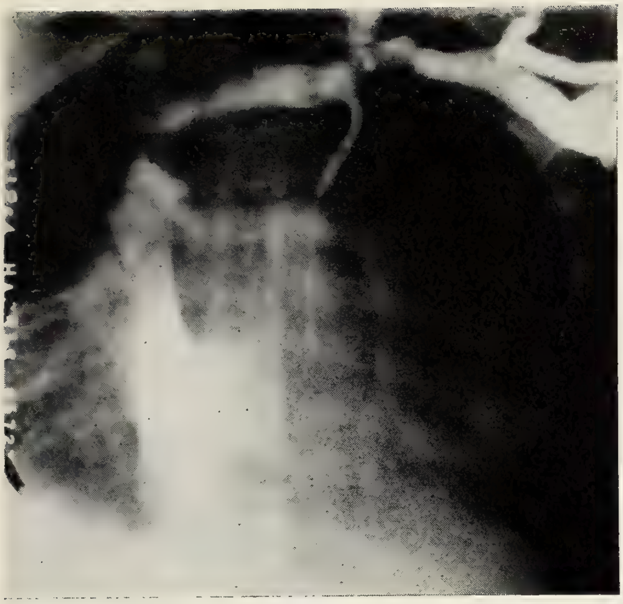

Figure 2

Venous angiogram taken on admission. Dye fills the superior vena cava, right atrium, right ventricle and main pulmonary artery. The marked increase over normal of the distance fom the right border of the cardiac silhouette to the right cardiac chambers is compatible with pericardial effusion. The chambers appear normal in size.

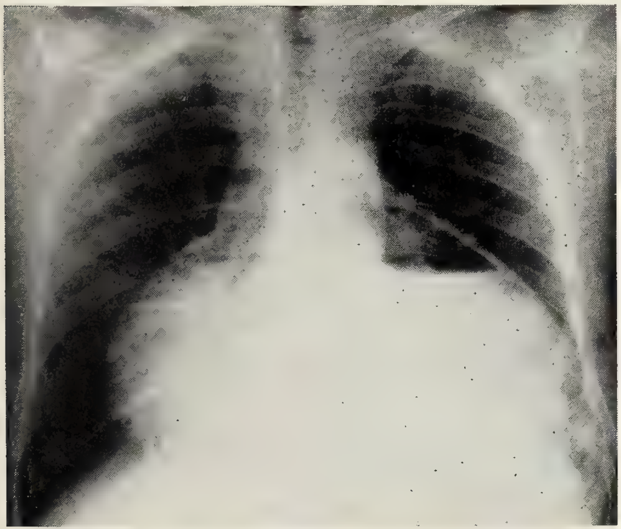

Figure 3

Radiograph of the chest following pericardiocentesis of 1500 ml and injection of 150 ml air.

space. On fluoroscopic examination the underlying heart size appeared normal. Following pericardiocentesis the venous pressure dropped to 90 mm saline and a diuresis began.

The pericardial fluid had a specific gravity of 1.030. It contained 7.6% protein; 2 ml packed red blood cells and 3 ml of packed white blood cells per 100 ml; 14,650 white blood cells per mm^3 and 12,200 red blood cells per mm^3. On light microscopy no cholesterol crystals were seen and the cholesterol content was 337 mg %. The fluid contained no tumor cells on cytological examination. Microscopic section of cell blocks made from spun sediment fixed in formalin showed a homogeneous mass of fibrinoid exudate with foci of fresh hemorrhage. No tumor cells, bacteria, fungi, or tubercle bacilli were seen on special stains. Cultures for bacteria, fungi, and mycobacteria were negative.

Before angiographic studies were performed, blood was obtained to confirm the suspected clinical diagnoses of myxedema and anemia. A PBI was 1.0 micrograms % normal 3-6 micrograms %). A serum liothyronine I^{131} (T3) uptake was 121% (in nonpregnant patients 93% or lower is compatible with hyperthyroidism: 107% or higher is compatible with hypothyroidism). A cholesterol was 506 mg % (normal 150-230 mg %) and a carotene was 468 micrograms % (normal 70-200 micrograms %). A photomotogram of the achilles tendon reflex indicated a markedly prolonged one half relaxation time of 720 milliseconds (normal 260-380 milliseconds). The patient was also found to be anemic with normocytic, normochromic indices. The hematocrit was 29% with 0.5% reticulocyte count. Serum iron was 53 micrograms % (normal 50-150 micrograms %) and serum iron binding capacity 382 micrograms %. Hematologic evaluation included the following normal studies: white blood cell count and differential; prothrombin time; clotting time; partial thromboplastin generation time; platelet count; hemoglobin electrophoresis; serum B12 and folic acid levels; and direct and indirect Coombs tests. Stool guaiac and benzidine tests were negative. Several attempts at bone marrow aspiration were unsuccessful.

Other laboratory tests included a normal urinalysis; three negative LE preparations; normal electrolytes and liver function tests, negative VDRL, and second strength tuberculin skin tests. The twenty-four hour 17 ketosteroid excretion was low on admission (1.8 mg per 24 hours), but a plasma cortisol was normal, and a normal sella turcica was seen on lateral skull films.

The patient's clinical course following pericardiocentesis and the institution of thyroid therapy steadily improved. Within three days orthopnea and dyspnea had abated, and after three weeks he had lost twenty pounds (Table I). During the first week he was given increments of desiccated thyroid up to two grains daily and a slow fall in serum cholesterol was noted. By the end of three weeks a remarkable diminution of cardiac size was found on radiograph of the chest (Fig. 4). 17 ketosteroid excretion rose to 4.8 mg per 24 hours, the achilles tendon one half relaxation time returned towards normal, as did the serum cholesterol (Table I).

The patient was discharged after three weeks of thyroid replacement therapy, but was readmitted three weeks later for reevaluation of anemia which had not improved. A bone marrow aspiration was successful and showed adequate iron stores with erythroid hyperplasia. The hematocrit was 27% with 0.9% reticulocytes. Ferrokinetic studies included a rapid Fe 59 plasma iron clearance of 38 minutes (normal 60-180 minutes) and two normal tests of Fe 59 incorporation into red blood cells (100% and 86%). Acid was present in gastric aspirate after histamine stimulation. No additional therapy was instituted, and after eight weeks of two grains of thyroid extract per day the hematocrit rose to 34%, and after twenty weeks of therapy to 40%.

The reflexes, heart size, and hematocrit remained stable on two grains of thyroid extract per day for 2½ years. However, six months ago, because of weight gain, tran-

Table I

Clinical Response to Thyroid Therapy

Elapsed Time from admission (in weeks)	Therapy	Weight (pounds)	Hematocrit (ml packed RBC) (100 ml blood)	Cholesterol (mg %)	Achilles Tendon* half relaxation time (milliseconds)
0	pericardio-centesis (1300 ml)	220	29	506	720
1	Thyroid Extract (2 grains)	210	27	450	–
3	"	200	27	415	400
6	"	200	27	215	340
8	"	206	34	–	–
20	"	208	40	–	–

*obtained by Photomotograph Test (normal 260-380 milliseconds)

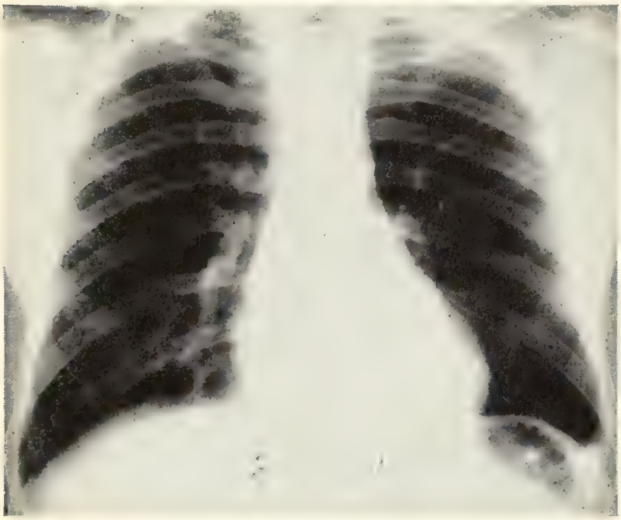

Figure 4
Radiograph of the chest three weeks after instituting thyroid therapy.

sient ataxia, increased serum cholesterol and carotene, and a PBI of 2.6 micrograms %, his thyroid dose was increased to three grains per day with resultant return to normal of these parameters.

Discussion

The patient presented as a medical emergency, and a detailed clinical history was obtained only in retrospect. Since hypothyroidism rarely causes pericardial tamponade the diagnosis might easily have been overlooked, but the presence of anemia, pallid yellow skin, and pendular reflexes suggested the possiblity of myxedema. Therefore, blood was drawn for iodine studies before iodinated radiographic dyes were injected, and chemical confirmation was obtained. The patient's clinical course fulfilled the criteria for "myxedema heart"[1-3]. The prompt diuresis, and fall in venous pressure after aspiration of only one quarter of the estimated effusion was attributed to the alleviation of tamponade. Within three weeks of thyroid therapy cardiac action returned to normal, the remaining pericardial effusion was reabsorbed, and the heart returned to normal size. Electrocardiographic changes[4-6] also reverted to normal, but not as quickly as cardiac action or size (Fig. 5). Low T waves became deeply inverted after pericardiocentesis and remained inverted during initial thyroid therapy, but became upright several months later. The QRS complexes of low amplitude did not increase in amplitude after pericardiocentesis or during the initial few weeks of treatment, but did increase after several months of thyroid therapy.

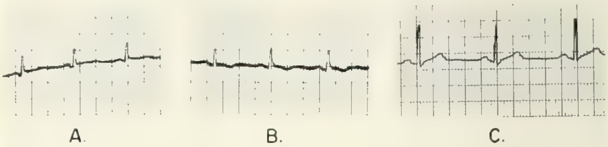

Figure 5
Electrocardiogram (Lead I)
(A) Low amplitude of QRS complexes and flat T waves obtained on admission.
(B) Inverted T waves observed following pericardiocentesis and during the first three weeks of thyroid therapy.
(C) Increase in QRS amplitude and return of upright T waves three months after thyroid therapy.

Although other laboratory signs of myxedema, such as hypercholesterolemia, hypercarotenemia, and pendular reflexes returned to normal after six weeks of therapy, a resistant anemia was not corrected for five months (Table I). Reported cases of anemia in myxedema characteristically required several months of thyroid therapy before returning to normal[8]. Rarely, however, did the anemia present with an hematocrit below 35%[8 9]. In this case, as was most common in other cases of myxedema, the anemia was normocytic and normochromic. No associated iron deficiency was found and there was no abnormality in iron incorporation into red blood cells, a finding recently commented upon in the literature[10]. The hematocrit of 27% was lower than expected, and the reduced red cell mass was probably caused by the combined effects of a lowered metabolic rate and oxygen requirement in addition to chronic bleeding into the pericardial space.

The most unusual finding in this case was the cardiac tamponade produced by a pericardial effusion containing old and new blood. The rarity of tamponade in myxedema has been explained by the slow formation of effusion and the ability of the pericardium to distend[5]. However, in other reported case of pericardial effusion due to myxedema the character of the fluid was quite different. It was straw colored with low specific gravity (1.012-1.025) and low protein content (3-5 gm %). Some white cells were reported, but red cells were not usually seen. In this case and in one other reported case of tamponade[7], the fluid was brownish-green with high specific gravity and protein content, and contained red cells, white cells, and products of altered blood.

How then could myxedema produce hemorrhagic pericardial tamponade? The deposition of mucopolysaccharides between endothelial cells of myxedematous capillaries offers a possible explanation. Increased capillary fragility has been recognized in myxedema and in fact has been used in the past in diagnosing hypothyroidism and its response to therapy[11]. More recently, gastrointestinal, cerebral, and mucocutaneous bleeding have been reported in myxedema coma and attributed to increased capillary fragility[12]. This patient gave a history of significant but mild, non-penetrating chest trauma, which could have produced slow bleeding into the pericardial sac because of underlying capillary fragility, creating, eventually, a large blood clot. This clot could have liquefied, produced smaller protein molecules, raised the intrapericardial colloid osmotic pressure, and attracted more fluid into the pericardial space[13]. If bleeding and liquefaction continued the volume of fluid would increase until the patient became symptomatic from cardiac tamponade. Pericardiocentesis relieved the tamponade and allowed diuresis to begin. Then thyroid therapy corrected the capillary fragility and prevented further capillary bleeding. Since capillary fragility and bleeding occur in myxedema the possibility of myxedema should be considered in hemorrhagic pericardial tamponade.

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Azotemic Renal Osteodystrophy

David M. Kessner, M.D.

Introduction

A variety of terms have been used to describe the skeletal complications of chronic renal disease. The association of florid bone disease and renal insufficiency was first noted by Lucas in 1883 who described the development of rickets in a child with albuminuria. This association was subsequently noted by pediatricians[2] and thus the terms "renal dwarfism", "renal infantism" and "renal rickets". It was not until 1937 that Albright and his colleagues[3] observed an adult patient with chronic renal failure and skeletal changes of osteitis fibrosa cystica that were indistinguishable from the bony lesions of primary hyperparathyroidism. In that same year Park and Eliot[4] recorded the occurrence of osteitis fibrosa cystica in children with renal rickets. It is now well established by histopathologic studies that renal rickets or osteomalacia are invariably associated with varying degrees of secondary hyperparathyroidism. Stanbury[5] has observed that, "among a group of patients with azotemic renal osteodystrophy, one may detect disturbances of almost all the biological processes that are known to involve bone as a tissue and bones as units of structure".

In the first comprehensive study of the metabolic abnormalities associated with this condition, Liu and Chu[6] used the term renal osteodystrophy. Subsequently, confusion arose because the bone lesions and disturbance of calcium metabolism associated with primary renal tubular defects (de Toni-Fanconi Syndrome, renal tubular acidosis), acute renal insufficiency, and the nephrotic syndrome[7] have been found to resemble the changes in patients with chronic azotemia due to renal glomerular disease. In 1957 Stanbury[5] employed the term "azotemic renal osteodystrophy" to distinguish the skeletal complications associated with chronic renal failure from those characteristic of primary renal tubular defects without azotemia. The renal lesions most commonly complicated by azotemic renal osteodystrophy are: 1) congenital renal disease including renal hypogenesis and polycystic disease; 2) obstructive urinary tract lesions; 3) chronic bilateral pyelonephritis; and 4) chronic glomerulonephritis.

Clinical Description

Symptomatic azotemic renal osteodystrophy is most often found in patients with long standing renal disease; the severity of the bony lesions seems to be correlated with the duration of the renal disease.[8] Although histopathologic evidence of bone disease is found in 50 percent of patients dying of renal failure,[9] clinically significant osteodystrophy occurs in only a small fraction of these patients. The usual presenting complaints are hip or shoulder pain, abnormal gait, painful and deformed terminal phalanges or metastatic calcifications. Roentgenologic evaluations frequently show only bony demineralization; however, in patients with changes of advanced osteitis fibrosa cystica the classic findings are sub-periostal resorption of the phalanges or brown tumor formation, while in those with more evident osteomalacia, pseudo fractures are noted. The increasing availability of chronic intermittent dialysis has allowed patients with virtually no renal function to survive for months or years. These patients seem to have a propensity to develop osteodystrophy and metastatic calcification which is probably a reflection of the severity and duration of their renal disease rather than a complication per se of hemodialysis.

Stanbury and Lumb[10] in an extensive survey of the plasma changes in patients with azotemic renal osteodystrophy, have classified patients according to the nature of the predominant skeletal abnormality into two groups: (1) those with defective mineralization in the form of rickets or osteomalacia; and (2) those with generalized osteitis fibrosa cystica. In general, patients with defective mineralization have a lower serum calcium and serum inorganic phosphate than those with dominant osteitis fibrosa cystica. Consequently the plasma (Ca) x (P) is higher in the latter group with a mean value of 86.5 in comparison to 45.7 in those with defective mineralization. The implications of this grouping of patients are important in the pathophysiology and treatment of patients with azotemic osteodystrophy.

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Pathophysiology

Figure 1 depicts our current concepts of the mechanisms controlling normal calcium homeostasis. Mc Lean[11] postulated that the mechanism controlling calcium homeostasis was a simple negative feedback system in which a decrease in serum ionic calcium stimulated the parathyroid glands to release parathyroid hormone which restored serum calcium to normal. The primary effects of PTH are: 1) to increase the renal proximal tubular reabsorption of calcium and inhibit reabsorption of phosphate; 2) to promote bone resorption and the release of skeletal calcium and phosphate; and 3) to act in the presence of vitamin D to facilitate the gastrointestinal absorption of calcium. The importance of the latter in man is unclear. These processes raise the serum ionic calcium and result in a net decrease in serum phosphate. The elevated serum ionic calcium was thought to suppress PTH release and thus the serum calcium was maintained within narrow limits. This theoretical mechanism adequately explained the persistence of induced hypocalcemia in thyroparathyroidectomized dogs but failed to account for the inability of thyroparathyroidectomized dogs to respond normally to an acute calcium load.[12] Copp and his co-workers[13] were the first to appreciate the implications of this finding and in 1962 postulated the existence of a hypocalcemic humoral substance, calcitonin, which they felt was released by the parathyroid gland in response to hypercalcemia. Intensive studies during the past five years[14] indicate that this substance now called thyrocalcitonin and identical with calcitonin originally described by Copp et al,[13] is a low molecular weight polypeptide produced by the thyroid gland. As depicted in Figure 1, thyrocalcitonin release is stimulated by relative ionic hypercalcemia and causes hypocalcemia and hypophosphatemia. This polypeptide has been isolated from the thyroid gland of man and many other species and appears to exert its hypocalcemic and hypophosphatemic action by inhibiting bone resorption.[15] The interaction of PTH and thyrocalcitonin in a dual feedback scheme (Figure 1) provide a reasonable explanation for the precise control of serum calcium in man.

The sequence of events leading to the deranged calcium metabolism of azotemic renal osteodystrophy have not been clearly or completely defined. Classic external balance studies by Liu and Chu[6], subsequently confirmed by others,[8] demonstrate that patients with renal insufficiency are in negative calcium balance. In untreated patients, the feces contain approximately the amount of calcium found in the diet and the total urinary content of calcium is negligible. This pattern was recognized by Liu and Chu to be similar to that seen in uncomplicated vitamin D deficiency rickets. They speculated that an "anti-vitamin D" compound might be circulating in the blood and were able to effectively treat some patients with high doses of dihydrostachysterol in the form of AT 10. It was subsequently shown that equipotent doses of vitamin D were equally effective in correcting the calcium malabsorption and treating the bone disease.

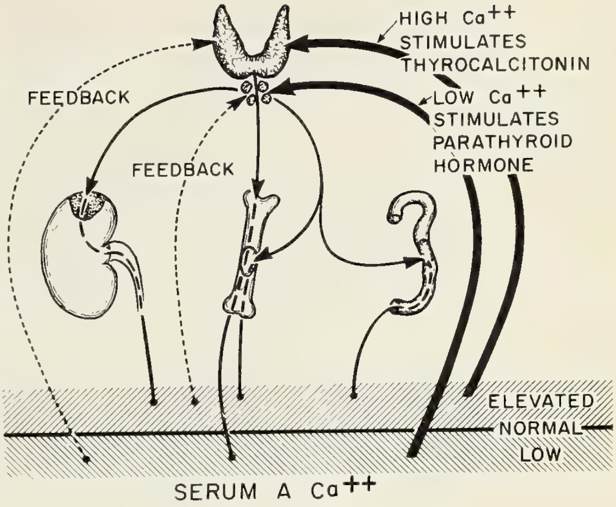

Figure 1

A scheme for the control of calcium homeostasis. See text for detailed explanation.

Although such an anti-vitamin D compound has not been isolated, there is much information to support this concept. Animal studies confirm the calcium malabsorption and demonstrate disordered calcium transport across the small intestine of uremic animals[16], a process dependent upon Vitamin D activity. Furthermore, Avioli and Slatopolsky[17] report that patients with chronic renal disease have decreased gastrointestinal absorption of radioactive labelled vitamin D, an increase in the vitamin D fractional turnover rates, and increased formation of biologically inactive metabolities of vitamin D. These derangements in vitamin D metabolism provide an explanation for the observed resistance to vitamin D in patients with chronic renal disease and are consistent with the hypothesis of a circulating inhibitor of vitamin D.

The hypocalcemia of chronic renal disease has been attributed to a primary elevation of plasma phosphate. This view is based on the work of Albright and his colleagues[18] demonstrating that the plasma levels of calcium and phosphate vary reciprocally in subjects with hypoparathyroidism treated with parathyroid extract. Subsequently it has been shown that this simple relationship does not always hold in patients with renal or other diseases and that a variety of factors protect the general constancy of the plasma (Ca) x (P) other than the simple precipitation and dissolution of calcium phosphate salts. It now seems clear that an important cause of the hypocalcemia of azotemic osteodystrophy is calcium malabsorption. This occurs early in the course of parenchymal renal disease, i. e. in patients with renal disease but without azotemia, and probably explains the hypocalciuria observed with minimal renal insufficiency. A tentative scheme to explain the pathophysiology of azotemic renal osteodystrophy is presented in Figure 2.

Gastrointestinal malabsorption (Figure 2) leads to hypocalcemia and a diminished serum ionic calcium which acts as a stimulus to parathyroid activity. The parathyroid glands become hyperplastic and the increased secretion of PTH results in bone resorption and the release of skeletal calcium. During the course of chronic renal disease, metabolic acidosis develops and calcium carbonate is released from bone to buffer the systemic acidosis. It is very unlikely, however, that this is a primary event as calcium metabolism is disturbed prior to the onset of azotemia and acidosis, and the bone lesions of azotemic osteodystrophy can be effectively treated with Vitamin D despite severe and untreated acidosis. Nevertheless, acidosis is another important factor contributing to bony reabsorption.

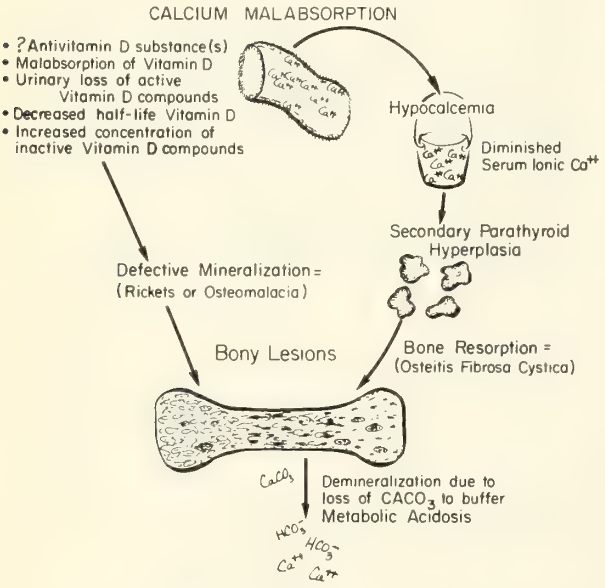
CALCIUM MALABSORPTION
• ?Antivitamin D substance(s)
• Malabsorption of Vitamin D
• Urinary loss of active Vitamin D compounds
• Decreased half-life Vitamin D
• Increased concentration of inactive Vitamin D compounds
Hypocalcemia
Diminished Serum Ionic Ca++
Secondary Parathyroid Hyperplasia
Defective Mineralization = (Rickets or Osteomalacia)
Bony Lesions
Bone Resorption = (Osteitis Fibrosa Cystica)
CaCO3
Demineralization due to loss of CACO3 to buffer Metabolic Acidosis
HCO3-
HCO3-
Ca++
Ca++

Figure 2

A model of the pathophysiologic events leading to azotemic renal osteodystrophy. See text for detailed explanation.

The majority of patients with symptomatic azotemic renal osteodystrophy take one of three courses which correspond to the classification of Stanbury and Lumb[10] referred to previously: 1) the largest group remain hypocalcemic and show predominant evidence of defective mineralization with rickets or osteomalacia; compensatory parathyroid hyperplasia is apparently not completely effective and thus they remain hypocalcemic but with primary evidence of their relative vitamin D deficiency and not secondary hyperparathyroidism; 2) another group of patients show near normal serum calcium values despite marked hyperphosphatemia; these individuals have osteitis fibrosa cystica and frequently metastatic calcification. It is assumed that parathyroid hyperplasia resulted in complete compensation with normal serum calcium but only at the price of symptomatic secondary hyperparathyroidism; 2a) the third group have been designated as having "tertiary hyperparathyroidism" or autonomous parathyroid function. These patients merge with group 2 and only differ in that their parathyroid function is no longer responsive to the physiologic control mechanisms. Thus the feedback mechanism shown in Figure 1 is no longer operative and increased parathyroid function continues despite elevation of the serum ionic calcium level to normal or supranormal levels. Some of these individuals present with hypercalcemia during the course of their untreated renal disease, while others develop it after renal transplantation. For reasons that are not clear the parathyroid glands have compensated too well and are no longer able to shut down when the normocalcemic state has been achieved. These patients show bone lesions characteristics of hyperparathyroidism and are thus a part of Stanbury's and Lumb's[10] group 2.

Differential Diagnosis

The patient with longstanding renal disease, bone pain and roentgen evidence of osteomalacia and/or osteoporsis presents no difficulty in diagnosis. However, in the uremic patient with predominant signs of secondary hyperparathyroidism one must always consider the possibility that occult primary hyperparathyroidism is the primary cause of the bone disease and that the renal lesion is secondary to hyperparathyroidism. In this instance, the past medical history is often of greatest help. A careful inquiry should be made regarding renal stones, peptic ulcer, pancreatis and, in mothers, of neonatal tetany in their children. Nephrocalcinosis should be searched for, as it is unusual for primary hyperparathyroidism to result in uremia in its absence. In those patients who present with normal or elevated serum calcium values it is difficult to exclude completely the possibility of primary hyperparathyroidism. Indirect estimates of parathyroid function such as calcium infusion tests or various measures of the renal clearance of phosphate are difficult to interpret in the face of renal insufficiency. Although PTH levels have been demonstrated by Berson and Yalow[19] to be extremely high in many cases of secondary hyperparathyroidism and only modestly elevated in the majority of primary adenomas, the overlap is too great to allow PTH assay to be used as a discriminating test.

Treatment

The rickets or osteomalacia of azotemic renal osteodystrophy usually can be treated effectively with vitamin D and supplemental oral calcium. The dose of vitamin D varies with each individual and must be controlled by measuring the serum calcium and adjusting it to achieve a normocalcemia state. An initial daily dose of 50,000 units of vitamin D with 1.0 to 2.0 grams of elemental calcium in the form of calcium carbonate (2.0 to 4.0 grams as the carbonate) is an effective regimen. The dose of vitamin D may have to be increased to as much as 250,000 to 500,000 units daily. Vitamin D not only promotes mineralization and healing of rickets or osteomalacia but removes the stimulus for secondary hyperparathyroidism. (Figure 2)

These Group 1 patients (predominant defective mineralization) must be carefully followed to avoid hypercalcemia and to watch for metastatic calcification. If a normal serum calcium level is achieved and the patient does not experience symptomatic relief of bone pain and develops further bone lesions or metastatic calcification, vitamin D and calcium should be stopped. These individuals have a greater component of secondary hyperparathyroidism than was orignally estimated and will not respond to vitamin D until substantial parathyroid tissue has been removed. Vitamin D therapy should not be used in patients who present with overt secondary hyperparathyroidism (Group 2) or autonomous parathyroid function (Group 2a) with a normal or elevated serum calcium, as in such patients vitamin D carries a substantial risk of increasing metastatic calcification and is usually unsuccessful in healing the bone lesions until parathyroidectomy has been carried out. The decision to perform a subtotal parathyroidectomy in such patients is based on several considerations: 1) the severity of the bone lesions and the extent of the metastatic calcification. The latter frequently involves peripheral, cerebral or coronary arteries and can in itself be life threatening; 2) the general health of the patient as it bears on their ability to withstand anesthesia and neck exploration. With careful attention to the problems of general anesthesia in the face of renal insufficiency and an experienced parathyroid surgeon, surgical mortality and morbidity are not limiting factors; 3) the planned program for treating the patient's renal insufficiency. The advent of chronic intermittent dialysis units and renal transplantation programs has altered the prognosis of the patients with renal insufficiency. If facilities are available for long term dialysis and/or renal transplantation, osteodystrophy unresponsive to vitamin D and oral calcium and with predominant osteitis fibrosa cystica should be treated early in its course with parathyroidectomy. In patients who are going to be maintained on hemodialysis, a strong argument can be made for total parathyroidectomy, as the remaining parathyroid remnant is still subject to the stimulus of renal insufficiency and can be expected to enlarge and eventually cause further bone disease and disordered calcium metabolism.[19] Total parathyroidectomy for secondary (renal) hyperparathyroidism has been carried out in four patients without untoward effect.[20] In those patients in whom renal transplantation will be attempted, operation should be carried out prior to transplantation to protect the transplanted kidney from possible damage by hypercalcemia and to insure that the patient is in optimal condition for transplantation. In these patients in whom the stimulus for secondary hyperparathyroidism will be removed, a subtotal parathyroidectomy should be considered. Whether total or subtotal parathyroidectomy is performed, post operative hypocalcemia is often severe and prolonged. Initially, intravenous calcium gluconate as a continuous drip may be required to prevent tetany. As soon as possible the patient should be started on oral calcium carbonate and adequate amounts of vitamin D (50,000-500,000 units daily) to prevent hypocalcemia and promote bone healing. A marked decrease in symptoms is usually noted within a few weeks and roentgenologic evidence of bone healing may be noted in several months.

Although attempts have been made to treat renal osteodystrophy by binding phosphate with Baselgel, the results are discouraging. Phosphate binding does effectively lower serum phosphate and may cause metastatic calcification to disappear. However, phosphate deprivation in itself can lead to rickets or osteomalacia and does interfere with bone healing in azotemic osteodystrophy.

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ON CARDIAC MURMURS

The clinical study of cardiac murmurs, within the last few years, has led to our present knowledge of the diagnosis of valvular lesions of the heart. By means of the organic murmurs it is positively ascertained that lesions exist in cases in which, without taking cognizance of the murmurs, the existence of lesions could only be guessed at. The absence of the organic murmurs, on the other hand, enables us generally to conclude with positiveness that valvular lesions do not exist. As a rule, to which there are but few exceptions, these lesions may be excluded, if there be no murmur. These are great results; but the practical auscultator of the present day need not be told that the clinical study of cardiac murmurs has led still further into the mysteries of diagnosis.—Flint, A.: On Cardiac Murmurs, *Amer J Med Sci* 44:29-54, 1862.

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President

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State—Member, Connecticut State Medical Society since 1935; Member, The Council of the Connecticut State Medical Society; Member, House of Delegates; Past Chairman, Committee on Rural Health.

National—Member, American Medical Association since 1935; Delegate to the American Medical Association, six years; Member, Committee on Welfare Services; Member, Council on Rural Health, 17 years, and Vice Chairman, four years.

Personal: Charter Member and Past President, Rotary Club; Board of Trustees and Chairman three terms) of the East Hampton Congregational Church. Married to Elizabeth McKenzie; four children, five grandchildren.

Norman H. Gardner, M.D.
President

THE PRESIDENT'S PAGE

That time of the year has come again. We have a new set of officers. How many of our members take part in their appointment? Indeed, how many of our members take any interest in affairs of Organized Medicine at all? The officers of the Connecticut State Medical Society are elected by those members who are interested enough to attend county meetings. These people elect the members of the House of Delegates, who in turn nominate and vote on the officers. A very democratic process.

County Society meetings are really quite poorly attended when one thinks of the percentage of members who should be present but are not. Surely this is a cause for concern. How can your officers be sure they represent the majority if they are elected by the minority? Further, it is difficult to know how to make a meaningful decision at times for the same reason.

Some counties are making it mandatory for members to attend a certain number of meetings or forfeit membership. This seems quite drastic at first glance, but in truth it is not. Who can complain when dropped from membership under these circumstances? Indeed, non-attendance indicates a complete lack of interest. We need active members. We must insist on active members.

These are trying times for medicine. We are entering whole new concepts of medical care. It is true that much of this is being thrust upon us without our consent, but this seems to make little difference. The doctors are expected to make it all work, somehow, and I predict they will.

In order to cope with present day third party involvements, we must bring to bear out best thinking. Medicine must speak with one voice, but only after careful discussion of all angles. In truth, this might be accomplished by a few, and the solution be pleasing to everyone, but this is not the best way. We must all put our shoulder to the wheel and push along to the best solution we can possibly make. Some group is going to decide how medicine is to cope with the present day, and it better be us.

Regional Medical Planning is a relatively new device which is becoming increasingly important. We have many of our people working in the various Task Forces. I believe every doctor in the state should keep abreast of the deliberations of this group. Most of us know that all the conclusions reached by the Regional Medical Planners will not be palatable to us, but if we keep our eyes on this agency we may make its reports much more in line with what the consumers of medical care should have and deserve.

Many changes are taking place in our world. Don't let us expect the Twentieth Century to accommodate itself to us. We must instead accommodate ourselves to the Twentieth Century. In doing so, however, let us hope we can have some influence on the final result. We must not seek to modify it selfishly, but rather for the great good of all.

I hope those who read this page will decide to become active in organized medicine and urge all they know to do the same. A strong Society is the best guarantee of the best possible medical care for all the people.

Norman H. Gardner, m.d.

FROM THE GENERAL MANAGER'S OFFICE

William R. Richards, m.d., *General Manager*
160 St. Ronan Street, New Haven, Conn.
Telephone 865 0587

Peter F. Villano
Director of Public Relations

Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS
COUNCIL MEETING
Wednesday, March 27, 1968

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Bradley, Grendon, Polivy, Brandon, Caplan, Fabro, Hess, Rogol, Cramer, Egan, Abbot, Spitz, Hastings, Shepard, Ayres, Grant, Wilson, Palomba and Granoff.

Also present were: Mrs. Lindquist, Mr. Villano and Dr. Richards.

Absent were: Drs. Gardner, Nolan, Jacobson, Jr., Johnson, Pelz and Roch.

II. ROUTINE BUSINESS

Life Memberships

It was VOTED to approve applications for Life Membership filed by the following eligible Active Members of the Society:

Robert B. Hiden, New Canaan (FCMA)—1968
Lillian E. Shaw, New Preston (FCMA)—1968
Joseph C. Barry, Manchester (HCMA)—1968
Hilda C. Standish, West Hartford (HCMA)—1969
Lester Q. Stewart, So. Yarmouth, Mass. (HCMA)—1968
Nicholas Samponaro, Torrington (LCMA)—1968
Mildred H. Clark, New Haven (NHCMA)—1968
Albert Quintiliani, Norwich (NLCMA)—1968

Date of Next Meeting

The next meeting of the Council will be held on Thursday, April 18, 1968, starting at 1:30 P.M.

III. OLD, NEW AND SPECIAL BUSINESS

Election of Student Member

It was VOTED to elect to Student Membership the following Connecticut resident who is attending medical school:

John Paul Gens, Jr., 416 West Road, New Canaan
George Washington University School of Medicine—1971
Pre-Med: Trinity College (Hartford)
Parent: John P. Gens, M.D.

Communication re "Tri-State Planning Agency"

It was VOTED to receive as information a letter from Governor Dempsey, in response to an inquiry by the Council, which stated that the development of, and Federal grant application for, a plan to establish a "Regional (Connecticut, Rhode Island, Massaschusetts) Health Resources Information System for Coordinated Planning and Management" had not been accomplished with any intent to exclude the voluntary health agencies from participation. It was noted, however, that the Governor did not say that the voluntary agencies had been consulted on an organizational level or that they would be invited to participate in the plan, should the application for a Federal grant be approved. It was further VOTED to ask the President to appoint a small ad hoc committee to review the proposed "Tri-State Plan" and to report its findings to the Council with recommendations.

Reports—Conference Committee with State Bar Association

Actions on a series of reports submitted by the Conference Committee were taken as follows:

(a) It was VOTED to approve a recommendation of the Conference Committee that the Society support a bill or bills to establish the medical examiner system in Connecticut when the 1969 General Assembly is in session. The Society supported similar legislative measures in 1967.

(b) It was VOTED to elect to membership on the Conference Committee for 1968-69 the following: Brae Rafferty, Willimantic, Samuel B. Rentsch, Derby, Marcus E. Cox, Waterbury, and William P. Arnold, Jr. Middlebury. The names of these added members will be published in the Delegates Handbook for the 1968 Annual Meeting. It was further VOTED to table action on the nomination of Irwin H. Lepow, Hartford, for membership on the Committee since Dr. Lepow is not yet a member of the Society.

Report—Delegate to the Medical Society of the State of New York (2/11-15/68)

It was VOTED to accept, with commendation, the report of E. Tremain Bradley, President, on his attendance at the 1968 Annual Meeting of MSSNY as a delegate from CSMS. Pursuant to acceptance of this report, it was further VOTED to request the Council's Subcommittee to Study and Revise the Bylaw to devise methods by which better relations (communications) between specialty groups and pertinent Sections of the Society can be developed, and to make recommendation to the Council concerning same. One section of Dr. Bradley's report indicated that MSSNY had this matter under consideration.

Resolution re Telephone Prescribing of Class A Narcotics

Having resolved (1/17/68) to promote appropriate action at the Federal level which would amend the Harrison Narcotics Act to permit the telephone prescribing of Class A narcotic drugs, provided that the pharmacist receives a written prescription for same from the physician within 24 hours, and having reviewed the actions recommended by several committees and officers, it was VOTED to forward the subject resolution to the Washington, D.C. offices of the AMA, with copies to Connecticut Senators and Representatives; also, to refer the resolution for consideration by the Council of New England State Medical Societies (meeting on April 28) with a recommendation that joint action be taken to implement its purpose. It appears doubtful that the AMA Washington offices could do more than advise the Society in this matter, since the AMA House of Delegates has twice defeated resolutions of similar nature and intent.

Resolution re Appointment of Secretary of HEW

Having been apprised that President Johnson has nominated Undersecretary Wilbur J. Cohen for appointment as Secretary of Health, Education and Welfare (a cabinet post) the Council took actions as follows:

(a) It was VOTED to adopt the following resolution:

"RESOLVED: That the Council of the Connecticut State Medical Society urge the American Medical Association to review its file on the health care philosophy of Wilbur J. Cohen and be prepared to present appropriate testimony concerning his nomination for the office of Secretary of HEW to the Senate Committee that gives primary consideration to such nominations."

Transmitted to Milford O. Rouse, AMA President, copies of the resolution will be sent as information to the secretaries of the component county medical associations of CSMS.

(b) It was VOTED to communicate strong disfavor for Wilbur J. Cohen's appointment as Secretary of HEW to all Connecticut Senators and Representatives, and to urge their support in opposing the confirmation of his appointment by the Senate; also, that copies of this communication be sent to the chairman of the appropriate Senate Committee and to the presidents of the constituent state medical societies of the AMA as information and for possible similar action.

Addition of Members to Ad Hoc Committee to Study Problems of Abortion

On recommendation of the PR Division and other sources, it was VOTED to appoint additional members to this Ad HOC Committee (which is also studying voluntary sterilization and artificial insemination) as follows:

George L. Cushman, North Woodbury—Generalist
James C. Johnson, Jr., Hartford—Psychiatrist
Charles E. Jacobson, Jr., Manchester—Urologist
Phillip E. Sumner, Manchester—Obstetrician-Gynecologist

Report—CSMS Committee with Connecticut General on Medicare B

An informal verbal report was received from Dr. Polivy and several other members of this Committee concerning the matters discussed at two joint meetings held in recent months. Connecticut General is utilizing computerized techniques to revise and refine the definition of comparable "charge areas" in the State, in consequence of which there have been some adjustments of prevailing levels of usual charges within some of the areas. Preliminary studies have been made of the patterns of patient care exhibited by individual physicians, particularly with respect to higher-than-average utilization of covered services on the part of some. These studies will be pursued and sample "profiles" on selected practitioners will be presented for review by the

CSMS component of the Liaison Committee. While the Society has not established a review committee at state level, it is felt that the CSMS liaison representatives could be helpful to CG by evaluating some of these situations and making recommendations regarding policies that might be adopted to deal with them equitably. It was VOTED to receive this verbal report as information, and to advise the component county medical associations of this function of the Liaison Committee as a "state-level review committee" and to invite the county association review committees to consult with it on problem cases they may be encountering. Dr. Martin reported on his efforts to help resolve a dispute that has arisen between CG and the Section on Dermatology concerning annual "limitations" on payments for certain repeated procedures, such as the serial removal of a number of multiple keratoses. Thus far, the question remains unsolved.

Policy re Releasing Information on Medicaid Payments

Having learned that the Commissioner of Welfare has been requested by a member of the press to release statistics on the amounts of Medicaid payments made to individual physicians, including the names of the physicians, the Council VOTED to advise the Commissioner of its disapproval of such releases being made because:

(a) Such statistics, accompanied by the name of physicians, would be subject to misinterpretation and misrepresentation by the press.

(b) Such statistics might appear to question the professional integrity and ethical practice of a physician so named and/or cause public defamation of his character.

(c) The knowledge that their names and the amount of Medicaid payments they received could be so released and so subject to misinterpretation might well discourage practicing physicians from providing the medical services necessary to the maximum benefit of the public.

Communication—Connecticut Academy of General Practice

In a letter from Francis Gallo, President of the CAGP, the Academy's Board of Directors expressed to the Council increasing "concern with the pattern of dual fee payments (to generalists vs. specialists) for services rendered to patients eligible for Medicare, and, since March 1, 1968, Medicaid benefits". The Board also referred to a policy adopted by the Society "several years ago" which opposed such dual payments being made by any third party payor. It was VOTED that the Council confirm to the CAGP Board of Directors its findings of September 14, 1967; i.e., that "a careful review of actions of the Council and House of Delegates during the past five years (has) failed to disclose any specific policy on dual fees (payments)", and that Connecticut General (administering Medicare and participating in the administration of Medicaid) "pays accredited specialists at a higher rate than generalists *only* when analysis of 'usual' charges demonstrates that the 'customary' levels of specialists charges are higher in the area of practice concerned".

AMA Regional Conference on Legislative Activities

Having received notice from the American Medical Association that a regional conference on legislative (stressing national) activities will be held in New York City on May 22, 1968, the Council VOTED to ask the President and Chairman of the Council to select up to four qualified and interested members to attend the Conference as representatives of CSMS. The travel expenses of two representatives will be reimbursed by AMA, and the Society will make such reimbursement to two others.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on March 27, 1968. Detailed minutes of the meeting are in file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

NEUROLOGIST—Board eligible, seeks clinical affiliation in Connecticut. Considerable experience in Internal Medicine, Neuropathology and Psychiatry. Connecticut license, military obligations satisfied.

PSYCHIATRIST—Board certified, 37 years of age, with extensive clinical and administrative experience, is interested in locating in Connecticut. Seeks (part-time) position in M.H. clinic or mental health center, in addition to private practice.

RADIOLOGIST—40 years old, Chief, university radiotherapy department. N.Y., Connecticut licensed. Interested in private practice of radiotherapy in western Connecticut.

"When you're finished with baby, maybe you can tell me what I can do about my extra pounds."

Get them while they're easily reversible.

Obesity doesn't happen suddenly. This insidious process has its beginning—and the chances of reversing it are better—during the *first 10 to 15 pounds of weight gain.* When a new dietary pattern must be established, consider the adjunctive use of BAMADEX SEQUELS. Combining the proven *anorexigenic* action of d-amphetamine with the *tranquilizing* effect of meprobamate, BAMADEX SEQUELS controls appetite throughout the day, usually with a single capsule daily.

Contraindications: Dextro-amphetamine sulfate: In hyperexcitability and in agitated prepsychotic states. Previous allergic or idiosyncratic reactions to meprobamate.

Precautions: Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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361-8

INTERNIST—Board eligible resident in internal medicine at the New York Hospital desires association with established groups or physicians in Fairfield County. Will be available July 1968.

Placement Opportunities

WANTED: Internist, —Board eligible, to associate with two busy young internists in modern spacious offices in a New Haven suburb. Excellent hospital facilities available. A fine opportunity for arpid growth. For further information, contact: Marvin P. Zimmerman, M.D., or Edward S. Scherr, M.D., 960 Main Street, Branford, Connecticut 06405,

GENERAL PRACTITIONERS (Internist or G.P.): Growing residential community of 12,000 in greater Bridgeport area has recently lost two family physicians and is desirous of obtaining at least two replacements. Hospitals nearby and staff appointments favorable. Fully equipped offices readily available for lease or purchase.

INTERNIST urgently needed for community near Hartford, Connecticut. Rapidly expanding eneral Hospital serving a population of 30,000 needs internist to head the Department of Medicine and establish a private practice. Outstanding opportunity will be partially subsidized by the hospital and will be welcomed by a friendly Medical Staff.

WANTED: Young pediatrician to join two internists and two general practitioners in a new medical building complete with laboratory and radiology services in a beautiful suburb of Hartford, Connecticut. Type of arrangement offered flexible.

NEEDED: PEDIATRICIAN—For area of 60,000 in Northwestern Connecticut which has lost two of its three pediatricians to retirement and clinical research. Ample office space in principal area city. Progressive local hospital has full range of specialty services. For further information, write or call: John Nicklas, Executive Director, The Charlotte Hungerford Hospital, Torrington, Connecticut 06790.

DERMATOLOGIST—Board certified or eligible to take over a well established practice in central Connecticut, virtually unopposed, in growing area of 100,000, excellent income. Will introduce.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

New Haven County

184th ANNUAL MEETING NEW HAVEN COUNTY MEDICAL ASSOCIATION

The 184th Annual Meeting of the New Haven County Medical Association was held at the Waverly Inn, Cheshire, on Thursday, March 28, 1968.

The meetings was called to order by the President, Dr. Bernard Burnham of Waterbury.

Among our honored guests was the President of the Connecticut State Medical Society, Dr. E. Tremain Bradley. In response to his introduction he commented on the unusually large turnout of members, which was gratifying and pleasing to him.

Routine business transacted at the annual meeting included committee reports. election of new members, and a slate of officers for the year 1968-1969.

President-Charles Verstandig, New Haven
Vice-President-Kurt Pelz, Wallingford
Clerk-H. A. Levin, New Haven
Councilor-Stewart Petrie, Derby
Associate Councilors-Kurt Pelz, Wallingford and
  Morris Granoff, New Haven
Member, Executive Committee-
  Bernard A. Burnham, Waterbury

A placque for the broadcast question and answer program "Medicine 1965-66-67" was presented to the Waterbury Radio Station WATR and to the Waterbury Medical Society.

There followed a series of ten minute talks as listed below:

Legislature: Isadore H. Friedberg, M.D., Newington

Compac: Francis Gallo, M.D., Winsted

Regional Center Task Forces: Frank K. Abbot, M.D., Waterbury

Medical Care Health Center: William R. Richards, M.D., New Haven

Medicare: E. Stuart McCleary, M.D., Wallingford (absent). For Dr. McCleary; Mr. Charles Shelly

Due Process in the Hospital: J. Alfred Fabro, M.D., Torrington

The Annual Meeting was followed by a social hour and dinner, at which time the holders of "lucky numbers" were recipients of valuable door prizes prepared by Dr. Elliott Brand and his Program Committee. These prizes included a portable television which was won by Dr. Frederick Treder.

Respectfully submitted.
H. A. LEVIN, M.D., *Clerk*

Special Article

Endocrine Effects of Psychotropic Drugs: III. Glucose Metabolism

Richard I. Shader, M.D., Myron L. Belfer, M.D., and
Alberto DiMascio, Ph.D.

Alterations of carbohydrate metabolism have been implicated as etiological factors in mental illness and have also been utilized in attempts to treat (e.g., insulin coma therapy) certain disorders. Further, it has been recognized that glucose metabolism is modified during stress, and that stress may trigger the onset of diabetes mellitus. In this third article in our series, we review some of the literature on glucose metabolism in mental illness as well as the sparse literature on the effects on glucose metabolism of the more commonly prescribed psychotropic drugs.

Although blood sugar concentration can vary with emotional state[1-3], and carbohydrate metabolism is disturbed in psychotic patients[4-7] the existing evidence does not support any consistent hypothesis in psychiatric patients. Lorenz[8] in 1922, noting "the prominent role claimed for the endocrine glands in carbohydrate metabolism and the variations from normal reactions in clear endocrine dysfunctions" suggested the use of sugar tolerance to investigate "internal gland disturbance" in certain mental diseases. Although the findings indicated that as a group mental patients, not on psychotropic drugs, had a normal response, there were deviations among the diagnostic classifications: catatonics showed an elevated curve-which to Lorenz suggested the "existence of considerable emotional tension" . . . with consequent "sensitiveness of the suprarenals", oversupply of epinephrine and an upset endocrine balance; simple deteriorating schizophrenics showed a low curve, and manic-depressive cases, depressed type, tended to show a higher than normal curve. In the latter diagnostic group the recent work on the relationship between depression and corticosterone[9] with its hyperglycemic effect, may be a contributory factor. Braceland[10] , reporting on the delayed response to insulin which was associated with a diabetic glucose tolerance test in schizophrenic patients, calls on a previously noted "anti-insulin" factor in schizophrenics. This diabetic curve was not confined to any particular type of schizophrenia. However, it was found more commonly when the schizophrenia was acute rather than "burned out". Recent animal data[11] suggests indirectly another mechanism: the increased levels of epinephrine or norepinephrine that occur with excitement or activity may promote a delay in insulin action. This is consistent with the observations of Braceland. In the untreated schizophrenic, the group most frequently studied, the etiology, causality, or specificity of abnormal glucose tolerance tests remains obscure.

The effects of psychotropic drugs on glucose metabolism have not been adequately clarified, but the possibility of an effect must increasingly be borne in mind in their use. The distinction between the drug-linked disturbances which have been reported and true diabetes is unresolved, but a difference in intermediary metabolism has been noted between them,[12 13] and associated clinical stigmata are not as apparent in the former[14].

Hiles in 1956[15], reported 1) that five patients developed transient hyperglycemia and glycosuria while taking chlorpromazine which remitted when the drug was discontinued; 2) that five previously controlled diabetics became unstable while on chlorpromazine, and 3) that two patients with

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DR. RICHARD I. SHADER, Associate in Psychiatry, Harvard Medical School; Lecturer in Social Relations, Harvard University; Senior Research Psychiatrist and Co-Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center.

DR. MYRON L. BELFER, Teaching Fellow in Psychiatry, Harvard Medical School; Resident in Psychiatry, Massachusetts Mental Health Center.

ALBERTO DIMASCIO, PH.D., Research Associate in Psychiatry, Harvard Medical School; and Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center.

normal fasting blood sugar levels and no glycosuria before chlorpromazine therapy developed overt mild diabetes during drug usage—which did not revert when the chlorpromazine was discontinued. These clinical findings led Hiles to question whether phenothiazines might cause diabetes mellitus. Charatan and Bartlett[16] reported that chlorpromazine caused abnormal glucose tolerance curves in schizophrenic patients. Similarly, Arneson[17] noted the diabetogenic effects of phenothiazines in a patient receiving a combination of chlorpromazine and imipramine and commented on seven other phenothiazine cases in the literature. Amdisen[18] performed glucose tolerance tests on a group of patients during long-term treatment with chlorpromazine, perphenazine and clopenthixol. Very few patients showed glycosuria or abnormally high fasting blood sugar levels. However, glucose tolerance tests of the diabetic type were found in 40%, 35%, and 15% of the patients on chlorpromazine, perphenazine, and clopenthixol, respectively.

Waitzkin[19] in a study of 359 ambulatory mentally ill patients in whom drug use was not specified, who were not known to have diabetes, found that 11.7% did have diabetes. This finding led to the speculation that the diabetes found may have resulted, either directly or indirectly, from pervasive and prolonged use of tranquilizing agents. Balter[20] reported that 30.4% of an unselected population of 767 neuropsychiatric cases could be designated as diabetic.

Thonnard-Neumann[14] recently reported an increasing prevalance of diabetes among psychotic women following the introduction of chlorpromazine (4.2% in 1954 to 17.2% in 1966). The data are suggestive of a specific relationship, implicating both dosage (greater than 100 mg/day) and duration (several months). This is supported by a 25% remission in hyperglycemia and glycosuria when the drugs were withdrawn or the dosages reduced. Thioridazine appeared less diabetogenic than chlorpromazine or perphenazine, as had been previously noted by Amdisen[18]. Several other variables are noted, leaving questions unanswered in this and other studies. In the affected group there was a higher percentage of diabetic relatives and the incidence of obesity was highest (a secondary, but perhaps crucial, effect of the use of phenothiazines). In this study, the diabetes was more prevalent in the upper age ranges, although the actual mean age of the diabetic group was lower. It should be remembered that many of the studies demonstrating abnormal glucose tolerances have been conducted in hospitalized neuropsychiatric populations which contain many elderly patients. The incidence of actual diabetes increases with age. Similarly, the normal aging process is accompanied by alterations in metabolic activity and decreased glucose tolerance, and elevations in fasting glucose levels may simply reflect age appropriate nonpathologic functioning.

The question of psychosis *per se* as a relevant variable in the etiology of diabetes is raised by the Thonnard-Neumann study and remains unanswered by virtue of conflicting findings in other studies. He found an increased incidence in paranoid schizophrenics, and as already noted, other diagnostic subtypes have also been linked to diabetes in other studies. A study by Efron and Balter[20] following their previously reported study, found that certain drugs within specific diagnostic categories, did have hyperglycemic effects. When patients were considered without regard to diagnosis, phenothiazine derivatives caused no apparent alteration in either glucose level or saccharoid content and only minimally altered glucose tolerance suggesting a complex drug-diagnosis interaction. The findings were that undifferentiated schizophrenics on thioridazine or piperazine derivatives had higher average blood sugar values (Folin-Wu) than paranoids or others (mostly hebephrenics). Those on chlorpromazine did not differ from either the paranoids or "other" schizophrenics, and those without medication had the lowest average values.

Animal studies have shown chlorpromazine to increase blood glucose levels and to counteract insulin hypoglycemia.[21-24 28 30] Yet it has also been noted[25] that chlorpromazine causes a mild hypoglycemia and does not prevent the hypoglycemia produced by epinephrine in the rabbit. Hasselblatt and Schuster[26] and Christy, Longson, Horowitz and Knight[27] found that chlorpromazine did not block insulin hypoglycemia, although it did block tolbutamide induced hypoglycemia[26] and insulin induced ACTH release[27].

The question of the practical significance of the above studies arises in the management of psychotic patients who have either preexisting diabetes, or in the evaluation of abnormal laboratory values in patients who might be seen by a physician for medical reasons while under psychiatric care. The following case illustrates the usefulness of phenothiazines in the short-term management of the diabetic patient with concomitant psychosis.

Case 1). Mrs. S. is a 48 year old, married, chronic paranoid schizophrenic, who had diagnosed diabetes antedating her psychiatric history. The patient's diabetes required insulin (20 u NPH) initially and was subsequently controlled on 1500mg of tolbutamide. During multiple acute paranoid psychotic exacerbations, her diabetes was prominent in her ideation. In rages, she would throw away her syringes in disgust and try to deny the fact that she had diabetes. In November, 1967, the patient was admitted to a psychiatric hospital in the midst of a paranoid episode. Two weeks prior to admission, she began having delusions that people were trying to kill her and her son. She would not eat food, because she thought it was poisioned. She failed to keep her medical followup appointments because of her suspiciousness of people (and doctors in particular). On the day of admission, she became quite violent, smashing everything in sight, and threw out her tolbutamide.

On admission, she was grossly paranoid and agitated, refused all medication and meals (believing them to be poisoned), and would not cooperate to give urines. Physical examination was within normal limits, but her blood sugar was 164, and urines varied between 4+ sugar (with negative acetone) to negative sugar (with 4+ acetone) during the first 48 hours (when obtainable). She was immediately given chlorpromazine, intramuscularly, to control her agitation and to initiate antipsychotic therapy. Shortly following this, the patient began to take her tolbutamide, and in fact, became reality-oriented to her diabetic management rapidly, while other areas of her psychosis remained relatively unmodified. After four days, she was able to take chlorpromazine orally, and her paranoid ideation lessened to the point that she would take adequate food such that her diabetes was in good control. Her acute psychosis subsided by the 21st day, and she was discharged on her regular dose of tolbutamide and 1000 mg of chlorpromazine daily. This relatively high dose of chlorpromazine was well tolerated and was necessary for this particular patient at that time. Mrs. S. has done well in followup, continuing on chlorpromazine and her usual dose of tolbutamide.

This case illustrates that diabetes is not a contraindication to efficacious use of an antipsychotic medication, and may, in fact, permit safer management, as long as one is aware of the potential influence of the medication in the individual case.

The effects of the tricyclic antidepressants on sugar metabolism are also controversial. Arneson[17] suggested that imipramine had a diabetogenic effect in her reported case, since her patient's glucose tolerance test returned to normal when imipramine and chlorpromazine were discontinued; it is possible that the hyperglycemic effect could have been associated solely with the chlorpromazine. By contrast, Kaplan, *et al*[31] found in five mildly diabetic patients, of whom four were mildly depressed, that imipramine produced a diminution in glycosuria which returned when the drug was discontinued.

Apropos of the above equivocal data on imipramine, the following case represents perhaps an extreme in the degree to which one must be concerned with the use of combinations of drugs when psychiatric care is related to medical management. It should be noted that no clinical studies of adverse effects of amitriptyline, another tricyclic antidepressant, on glucose metabolism have been reported, and that its effect alone or in combination with the trifluoperazine cannot be stated unequivocally. We offer this case, however, to alert clinicians to potential difficulties.

Case 2). Mr. B. is a 30 year old, single, male who first presented for psychiatric care four years after the onset of diabetes mellitus. In the interim, the patient evolved from schizoid symptomatology to frank schizophrenia. After the onset of diabetes, noted after an episode of acidosis, he felt "very restricted", and subsequently was unable to sustain any goal directed activity. His diabetes was managed with difficulty because of his poor cooperation. He required high doses of both regular and NPH insulin. He tended to manipulate his parents with diabetic needs, about which he was "careless" when he felt lonely. He sought psychiatric help to lessen his progressive confusion. Following a thorough medical review by his clinic, he was started on 6.0 mg of trifluoperazine daily, later raised to 10 mg daily, by his psychiatrist. He did not appear depressed. Three months later the patient ingested ten Coricidin tablets when he became lonely, desperate, and angry at his parents' temporary absence. This precipitated a diabetic coma that required admission to a general hospital. He denied suicidal intent, saying that all he wanted was "more tranquilization".

Following discharge, he was continued on trifluoperazine (10 mg daily) and amitriptyline (25 mg orally three times a day). This was instituted because of feelings of "restlessness and depression". One week later, the patient was found by his sister in insulin shock that responded to Glucagon. Mr. B. said that at this time he had taken only four extra units of NPH (as he had been told to do) because he was working at night. He denied any attempt to harm himself. This raises questions about the role of amitriptyline in the production of the insulin reaction. The problems of management in this particular patient are illustrated by some additional history. Shortly following this incident, he discontinued the amitriptyline on his own, and took some chlordiazepoxide provided by his sister with magical expectations that it would "dull my feelings and stop my self-concern". In two weeks time, he took an "overdose" of chlordiazepoxide to get away from the "feelings of others". The patient said that when he became isolated, felt lonely or trapped, he either became "impulsive" about taking overdoses or neglected his diabetes. At this point, he was admitted to the Massachusetts Mental Health Center.

There is general agreement about the actions of monoamine oxidase inhibitors (MAOI), both hydrazines and nonhydrazines, on glucose metabolism. By altering monoamine metabolism they enhance glycolysis which is reflected by increased pyruvate and lactic acid levels and decreased glucose levels.[32] In 1959 Weiss, Weiss, and Weiss[33] reported the hypoglycemic effects of MAOI in man, as did Leak and Dormandy[34] a few years later. Van Praag and Leijnsf[35-37] showed that the therapeutic effect of hydrazine MAOI was accompanied by a decrease both in fasting blood sugar levels and in the blood sugar values attained after oral administration of glucose. The antidepressant effects were found to be related to the glucose effects—therapeutic failures showed minimal glucose changes. In subsequent papers[38] these same authors reported that a number of patients with depression have subnormal uptake of glucose such that they respond well to hydrazine MAOI antidepressants. In addition, they showed that when such patients improved with electroconvulsive therapy, the improvement was accompanied by a return of the glucose level to normal[39]. Cooper and Ashcroft[40] suggest caution when MAOI drugs are given to depressed diabetic patients who are also receiving insulin. They found that the hydrazine MAOI drugs potentiate, as well as prolong, insulin induced hypoglycemia in rabbits, whereas nonhydrazines appear only to prolong the insulin induced reduction in blood glucose. However, Ferrero and Marioni[41] found that nialamide decreased the effect of insulin on fasting blood sugar levels and had no appreciable effect on fasting blood sugar levels in the absence of additional insulin. Wickstrom and Pettersson[42] treated 35 patients who were diabetic and depressed. They found that MAOI drugs, pheniprazine and mebanazine, made it possible for some patients who had become refractory to sulphonylurea derivatives, to resume successful use of the sulphonylureas. However, most patients became hypotensive after about three or four weeks, coinciding in time with the onset of hypoglycemic effect.

Adequate published clinical studies on the effect of the minor tranquilizers on glucose metabolism were not found in our search of the literature. The following animal studies indicate their possible influences on glucose metabolism. Rutishauser[28] found that chlordiazepoxide produced shortlasting increases in blood glucose levels in rats. Fasted rats showed increased blood glucose after oral chlordiazepoxide[29]. The increases were related to the size of the dose and degree of sedation. Slight elevations were noted with diazepam while relative decreases were noted with meprobamate. It was also observed that other, more sedating investigational benzodiazepines did not cause increases in blood sugar levels. Marked increases were also noted with chlorprothixene. Optiz[30] also noted elevated blood sugars in starved rats receiving chlorprothixene, while meprobamate did not produce such increases.

The use of psychotropic drugs has been of unparalleled value in the management of psychiatric illness. The above data is presented to indicate in part the complex nature of the drug-host interaction and to emphasize the need for an understanding of their possible effects on glucose metabolism. Cautious use of drugs is indicated in diabetic patients. When serious doubts exist, an alternative such as in the following case should be utilized until full evaluation is possible.

Case 3.) Mrs. K. is a 37 year old, divorced, mother of one, who had her first psychiatric hospitalization ten months after the clinical onset of diabetes. From the outset, it was difficult to regulate her insulin requirements. Through efforts of her physician and social worker, with whom she became quite close, it was possible to maintain her on diminishing doses of insulin and finally on an oral hypoglycemic agent. She was hospitalized two weeks prior to psychiatric hospitalization with a urinary tract infection. Her diabetes was out of control. The patient was depressed at this time, and refused to eat (to the point of dehydration) or carry out a medical regimen. Her feeling was that if a good diet makes the illness more manageable, starvation will make it go away. She had fears of mutilation, blindness and death as complications of her illness. This was reinforced by observations of her mother's diabetic course. She refused an antidepressant. As the medical service felt she was refractory to supportive care with her depression, she was transferred to a psychiatric hospital.

On admission, she was depressed in a retarded fashion, but not psychotic. Her blood sugar for 24 hours ranged from 168 to 320. During the first day she refused food and would not give urines. When the staff convinced her of their intent to take care of her and were firm, she began to eat and cooperate in her management. She was managed in a conservative fashion with regular insulin and then switched to NPH. It became clear that she used her illness to draw people near. It was noted that she would starve herself to the point of insulin reaction when her doctor was away or to attract a nurse's attention. The patient felt that people who were important to her were more concerned when she was ill.

Some insight into her manipulation of "caring" people was gained through her work with her psychiatrist. She was able to elucidate a longstanding conflict with her mother over dependency, and the issue of the fear of mutilation from diabetes that had aroused other childhood fears. The patient was oriented to psychotherapy for amelioration of these concerns and she readily consented. After ten days, she had gained 10 lbs., her appetite returned, and she was less depressed. No antidepressant was used. She was referred back to her medical doctor for outpatient management, and outpatient psychotherapy at her general hospital was arranged.

In summary, phenothiazines have a hyperglycemic effect in some patients. Phenothiazines cannot, at this time, be considered to be causes of diabetics mellitus, but they may alter the threshold and thereby expose latent or prediabetic patients. It remains to be explained why neuropsychiatric patients, in general, appear to have a higher incidence of blood glucose elevations than in the general population. There may be meaningful drug-diagnosis interactions. Benzodiazepines also may increase glucose but probably even less frequently than the phenothiazines, while meprobamate does not appear to cause such increases. Tricyclic antidepressants may lower blood glucose, particularly in diabetic patients. This hypoglycemic effect is clearer with MAOI drugs and may represent a potential hazard if such drugs are given to patients who are concomitantly receiving insulin or sulphonylurea derivatives.

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Congress On Medicine And Insurance Announced

The close link between clinical and life insurance medicine will be explored by a congress on medicine and insurance to be held in San Francisco on June 15.

The meeting, co-sponsored by the Association of Life Insurance Medical Directors of America and the American Medical Association, is the first such meeting of the two organizations.

The congress, which immediately precedes the AMA annual meeting, will be highlighted by a morning panel of insurance company medical directors offering their views of clinical medicine.

Dr. Milford O. Rouse, president of the AMA, will speak in the morning on the mutual concerns of the medical profession and insurance companies in the area of clinical and insurance medicine.

The morning's panelists will review underwriting problems posed by people with serious ailments. Presentations will be given on heart disease, cancer, diabetes, obesity, tension, strokes and the like. The panelists are:

Dr. Richard S. Gubner, director of the diagnostic services division of the Equitable Life Assurance Society of the United States (New York City); Dr. Harry A. Cochran, Jr., vice president and chief medical director of Lincoln National Life Insurance Co. (Fort Wayne, Ind.); Dr. D. Sergeant Pepper, senior medical director of Connecticut Mutual Life Insurance Co. (Hartford); and Ardian Gill, F.S.A., vice president and actuary of The Mutual Life Insurance Co. of New York.

Other featured speakers include Howard A. Schneider, Ph.D., acting director of the AMA's Institute for biomedical research, and Dr. Albert L. Larson, vice president and chief medical director of the Travelers Insurance Co. (Hartford).

Dr. John O. Alden, medical director of Aetna Life Insurance Co. (Hartford), and Dr. Frederick J. Newirth, medical director of Fireman's Fund American Life Insurance Co. will discuss disability insurance — its underwriting and claims, and aspects of rehabilitation.

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Reminder

The Woman's Auxiliary to the American Medical Association Convention will be held June 16-20 in San Francisco, California. Make plans now to attend. There is a program for pre-teens and teens of Auxiliary members, sponsored by the Woman's Auxiliary. Complete details of this program will appear in the May issue of MD's Wife.

LEGISLATION

Did You Know

Since the founding of our country physicians and their wives have been a force in government and politics. Twenty-eight physicians served in the Continental Congress in 1774. Five physicians signed the Declaration of Independence.

The first governors of Delaware, Kansas, Connecticut, Ohio, and Alabama were physicians, and the ninth president of the country, William Henry Harrison was a physician. From Auxiliary News, Missouri.

Legislation—What Every Member Should Know

Lobbying. The right of individuals to engage in legislative activities is guaranteed by the first amendment to the Constitution. Any individual is free to lobby on any issue which is of interest to him. Only those persons engaged for pay in influencing federal legislation are required to register with the Congress.

The AMA maintains a staff of six active lobbyists in Washington who contact the 535 members of Congress. Contrary to what you may have heard or read, the AMA has only twice in the last 10 years been among the "top 10" for lobby expenditures.

Legislative Policy. Interest has existed since the first meeting of the AMA in 1848 when it recommended to Congress that it enact legislation providing for the appointment of inspectors at ports of entry to examine imported drugs and medicine. In 1898 the formation of a permanent legislation committee was suggested to the AMA House of Delegates.

In recent years the AMA has been a moving force in the passage of constructive legislation in the health field: Kerr-Mills, Hill-Burton, pure food and drug laws, medical school construction, drug abuse controls, water and air pollution laws, etc. Although medicine has a vital interest in legislation, the AMA spends less than 1 percent of its annual budget on these activities.

The AMA is sometimes accused of standing in opposition to most medical legislation introduced in the Congress. Examination reveals, however, that the AMA supports far more than it opposes. It supported 21 bills, opposed seven and gave partial support to five. During the 89th Congress (1965-1966) the AMA spoke out on 33 legislative proposals.

Each bill of medical interest is studied by the AMA's 13-member physician Council on Legislative Activities. The national auxiliary legislation chairman sits as liaison to this council which reviews legislation in view of Association policy, and makes its recommendations to the AMA Board of Trustees for their consideration. All AMA statements to Congress on pending legislation, or other matters, are based upon the policies established by the Board of Trustees and the 238-man House of Delegates.

Advises Mrs. Lyle F. Murphy, national legislation chairman: "When considering AMA policy, it is important to remember that the AMA is a scientific organization whose primary purpose is to advance the art and science of medicine. The AMA measures all proposals as to their probable effect on the physician's ability to render the highest possible level of medical care, and to determine such care solely on the basis of his considered medical judgment. The AMA feels that it is incumbent on it to stridently

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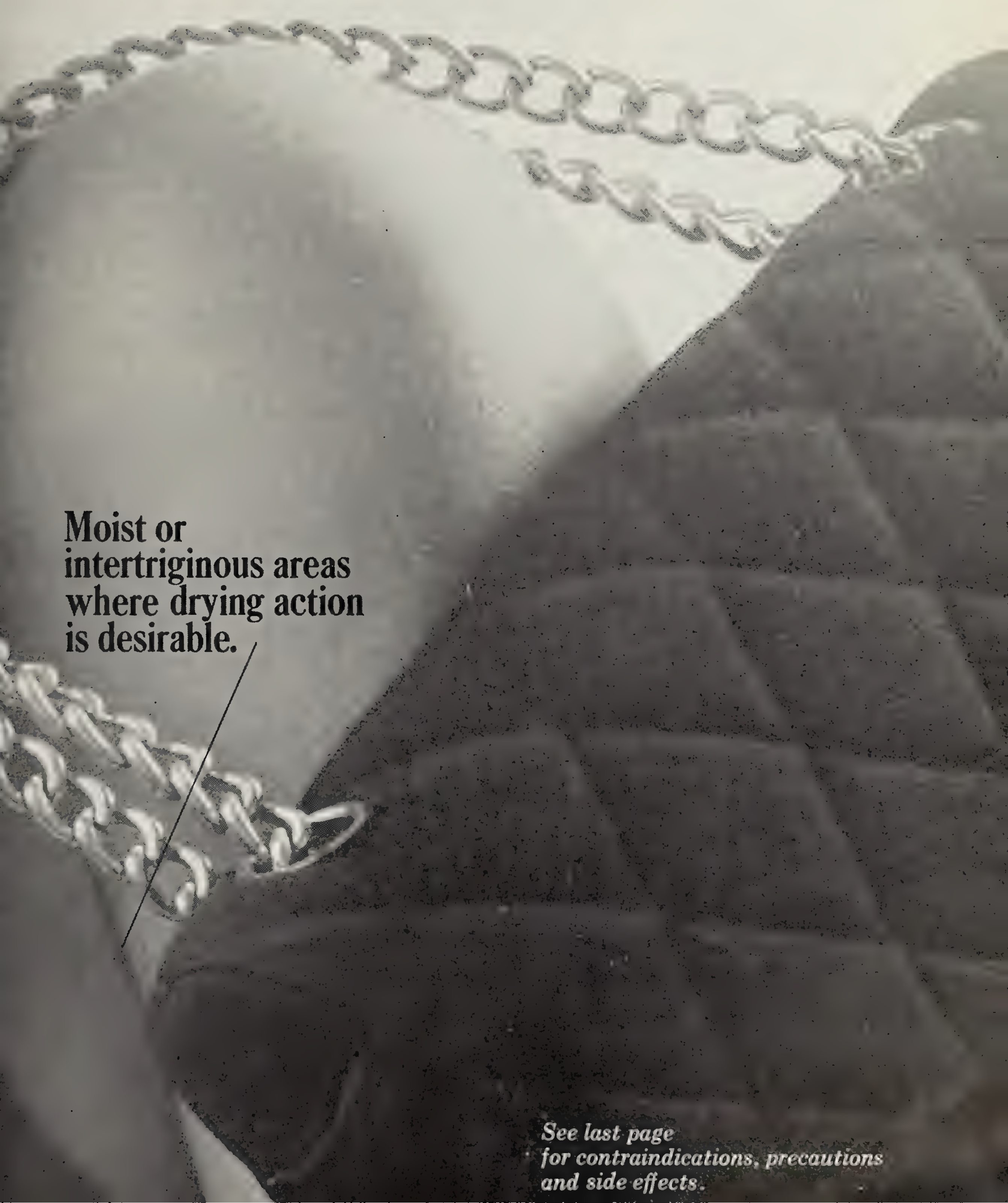

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In many areas of the body, hair gets in the way of treating the underlying dermatitis. The propylene glycol vehicle of Synalar Solution permits penetration and dispersion at sites where creams and ointments do not readily penetrate. May be applied without matting of hair.

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Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components.

Precautions: In some patients with dry lesions, the solution may increase dryness, scaling, or itching. Application to denuded or fissured areas, such as genital or perianal sites, may produce a burning or stinging sensation. If this persists and dermatitis does not improve, discontinue medication. Although propylene glycol has antiseptic activity, there should be careful initial evaluation and follow-up of infected sites. Incomplete response or exacerbation of lesions may be due to true infection, which requires susceptibility testing and appropriate therapy. On the other hand, saprophytic or low grade infections may clear spontaneously under the influence of Synalar Solution alone. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

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oppose all schemes which would adversely affect medical care, and to support with equal vigor all proposals which will lead to better medical care of the American people."

1968—A Big Year In American Politics

Few activities are more important to auxiliary members than participation in our political process, for not only as citizens but as women particularly concerned with the nation's health we have a stake in the election of the best people available.

Auxilians owe it to themselves and their husbands to at least register and vote in all elections including the primaries.

Direct Line—WA to the AMA

A good program next year might be "What Every Woman Should Know About Politics". Get a good speaker and invite others to your meeting.

Stress legislation in the coming year as you plan.

Mrs. Clarence W. Harwood

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.

Physical Standards In World War II. Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army. Editor-in-Chief, Colonel Robert S. Anderson, MC USA. Editor for Physical Standards, Charles M. Wiltse, Ph.D., Litt. D. Office of the Surgeon General, Department of the Army, Washington, D.C., 1967. 356 pp. $3.00.

Heredity, Disease and Man: Genetics in Medicine. Edited by Alan E. H. Emery, M.D. University of California Press, Berkeley and Los Angeles, 1968. 247 pp.

The Balkan Nephropathy. Ciba Foundation Study Group #30. Edited by G.E.W. Wolstenholme and Julie Knight. Little, Brown and Company, Boston, 1968. 125 pp. with 29 illustrations. $3.50.

Communication in Science: Documentation and Automation. Ciba Foundation Volume. Edited by Anthony de Reuck and Julie Knight. Little, Brown and Company, Boston, 1968. 288 pp. with 14 illustrations. $12.50.

Cell Differentiation. A Ciba Foundation Symposium. Edited by A.V.S. de Reuck and Julie Knight. Little, Brown and Company, Boston, 1968. 272 pp. with 33 illustrations. $12.00.

Health of Mankind. Ciba Foundation 100th Symposium. Edited by Gordon Wolstenholme and Maeve O'Connor. Little, Brown and Company, 1968. 312 pp. with 38 illustrations. $12.00.

In Memoriam

Carroll, William E.—Elizabeth, New Jersey; Dartmouth Medical School, 1914. Dr. Carroll served in the Medical Corps, U.S. Army and had practiced at Undercliff Hospital in Meriden, prior to moving to New Jersey. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was a Diplomate of the American Board of Internal Medicine. Dr. Carroll died February 27, at the age of 78.

Zeman, Burnhardt—West Hartford; University of Louisville School of Medicine, 1908. Dr. Zeman was a founder of the Mt. Sinai Hospital and a general practitioner in the Greater Hartford area for 58 years. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Zeman died March 26, at the age of 86.

Doctors Wanted To Work With Medical Mission In Underdeveloped Nations Of Africa

A Connecticut physician interested in humanitarian services, adverture, and travel is being sought by the directors of Operations Crossroads Africa Une to head up the U.S. AID founded medical project in Dahomey for a period of one year, beginning August 1.

The Chief of Mission of the Medical Service Program earns a salary of $10,000 and may have his family with him. Transportation and housing expenses for himself and his family will be paid by Crossroads Africa, administrator of the medical aid program under contract with the U.S. Agency for International Development.

Also sought for service in the Dahomey medical mission are two other physicians to serve as volunteers for three-month tours of duty each, effective August 1. The Short-Term Volunteer Physicians receive no salary. However, all transportation, housing and living expenses are paid by Crossroads Africa.

This is an opportunity for members of the Connecticut State Medical Society to help promote international goodwill by using their skills to advance the level of health care in the underdeveloped nations of Africa.

General practitioners and internists are desired but other specialists are invited to apply. Contact: David S. Brown, M.D., Director, Crossroads Africa, 173 East Avenue, New Canaan, Conn., Phone 966-4593.

64th AMA Annual Congress On Medical Education

February 11-12, 1968, Chicago, Illinois

The first day of the 64th Annual Congress on Medical Education of the American Medical Association was devoted to the need for increased manpower in health services and to the desirability of continuing medical education of physicians already in practice. Both of these, it was stressed, are necessary in order to improve the quantity and the quality of medical care in our country.

The term "health services" does not mean physicians' services but rather those rendered by the allied, or paramedical, professions, such as nurses, physiotherapists, social workers, and technicians of all sorts. In 1900 two of our three "health workers" were physicians; in 1964, only one out of fourteen had an M.D. degree.

Population growth is not the only cause for increased demand for medical services. Also to be considered are up-grading of "taste" or "medical sophistication," if you will, of the average citizen, his increased income, and governmental medical plans and coverages. Changes in medical care are also responsible. No longer does the physician, although he may still be (and, we hope, is) the "captain of the team," take complete care of his patient, especially the very ill one or diagnostic problem, in the hospital. Nor can he do so and practice modern medicine. With the developments of refinements in diagnosis and treatment, he may need a whole corps of people in "allied health services," such as nurses, technicians in perhaps several laboratories, and physiotherapists, to help him.

So there is need for more manpower and for more facilities for the training of this manpower. With these will come better distribution of services and improved co-ordination and planning to assure this distribution. If nurses spend forty per cent of their time performing non-professional duties that could be done by other personnel (as they do in many hospitals), then forty per-cent of nursing time is wasted. More rational division of labor will increase the productivity of health services and markedly reduce their cost.

In addition to the need for better division of labor, there exists the problem of shortages in some well-established fields of medical care. For example, New York City is budgeted to pay five thousand registered nurses but employs only approximately thirteen hundred.

Health is said to be the third largest industry in the country, and it is estimated that by 1975 there will be twenty-five supporting health personnel to one physician. Hence the problem of education and training of all of these groups (and many categories exist) arises. The hospitals, already overburdened, can no longer be expected to train the number or absorb the cost of the personnel needed. This is all being studied by the new A.M.A. Council on Allied Health Professions and Services, and it is felt that junior colleges may well prove to be the answer. The shortage of manpower, already alluded to, makes rapid recruitment, training, and planning extremely urgent, as our Government has decided that the mandate of society is comprehensive health care for all. Many programs, in colleges, junior colleges, and medical schools, are under way, and pilot programs and new curricula will be needed. This will be "occupational education" as distinguished from conventional collegiate academic training. The problem will arise as to which programs are academic enough to deserve a degree and which are purely vocational, involving mainly manual skills. In order to attract students, jobs obtained at graduation must be careers.

About nine hundred and twenty-three junior colleges are now in operation; one is being opened almost every week. These institutions will offer two-year courses, and their students will consist not only of high school graduates, but also of adults, as many are returning to school. Evaluation and some supervision of the programs must be done by professional groups. At present, the source of teachers is the professions and some members of hospital organizations working part-time.

Problems of licensure may well arise in these new professions. The original purposes in licensure were to set standards of competence in a profession, to protect both the profession and the public from incompetency, to give prestige to the profession, and, very probably, to limit the number of these entering it. It is felt by some that licensure no longer fulfills these purposes. For one thing, we now need to increase numbers rather than to limit them. One speaker argued that graduation from medical school, law school, or nursing school, now that all of them are similar in standards and curriculum, should be adequate to permit practice, that examinations are a "waste of time," that their results can be misleading, and that continuing regulation of medical practitioners is best done by hospital staffs, courts of law, and the insurance industry. Obviously, this attorney knew little of the problems connected with medical licensure. It is held that unauthorized practice is much less of a problem than poor practice. So much for the "established professions." However, it is admitted that the problem will be different in newer fields of endeavor, as standards must be set.

The "health team" approach to medical education and care involves an integration of all disciplines of health care. Such a program is now under way at the University of British Columbia and is participated in by medical students, student nurses, and so on.

Stressed in several presentations was the need for continuing medical education of the physician in practice. It is felt by some that many doctors do not keep up with the rapid advance of today's medicine, with its new techniques, new skills, and swiftly accumulating store of new knowledge. The gap between laboratory development and clinical application is disappearing. Tied in with this problem is, of course, the question of "medical competence." How is this competence to be evaluated? Various possible solutions were offered, among them the physician questionnaire, utilized in Utah. This questionnaire really amounts to a physician's own "medical inventory," so to speak; in his replies he furnishes an estimation of his needs, outlines his problems, and identifies areas of difficulty. Another suggestion made was periodic re-examination and recertification of members of the medical profession.

In addition to the usual forms of postgraduate medical education, such as literature, staff meetings, medical society lectures and occasional short refresher courses, the use of new media, such as television, was suggested. A National Library of Medicine, a National Audio-Visual Center connected with it, and a National Hospital, where films could be taken and postgraduate medical education obtained, were among the proposals. Computerized data available on call to physicians would aid in solving suddenly arising problems.

Since innumerable well-trained, Board-certified specialists have departed from university hospitals in the past twenty years, I fail to understand the surprise admitted by one of the speakers when he found "sophisticated, skillful practice" in many community hospitals without university affiliation. University hospitals have more tenure problems and a more complicated power structure than do community institutions. As only one-tenth of one per-cent of every thousand patients is admitted to university hospitals, it is obviously necessary that a high level of patient care be maintained in community hospitals.

Although there has been much talk about physician evaluation, little, allegedly, has been accomplished. Various means of evaluation, such as giving of tests, sometimes both before and after those examined have taken a given postgraduate course, direct observations of skills, and review of charts and records, in office and hospital, have been proposed.

On the second day of the Congress, various subjects were discussed: Patterns of utilizing multiple community resources, Specialty Board policies, governance of medical schools, and the current crisis in medical education.

In several cities (Pittsfield, Massachusetts, Jacksonville, Florida, and Wilminton, Delaware), two or more community hospitals banded together for economic pooling of resources and joint-staff participation in intern and residency training. Coordination of services and of libraries was achieved, and eventual corporate merger and university affiliation followed. The situational details were described at length. These moves led to elevation of educational standards that would not have been possible in any one of these institutions alone and also resulted in operational economies and elimination of duplication and triplication of effort, thus conserving health and manpower resources. Because of the increased educational opportunity and because of the university affiliation, it then became easier to attract house officers.

Residency Matching Programs in Psychiatry and Pediatrics were then reported on by two discussants. Difficulties were reported. In Psychiatry, only one-third of the residency applicants were enrolled in the Plan, and in Pediatrics, although two-thirds of the Services were in the Plan, it covered only one-third of the available positions.

In Internal Medicine, a uniform appointment and subsequent acceptance date for first-year residents have been set by the Association of Professors of Internal Medicine. Eighty to ninety per-cent of residencies are covered by this agreement, which is a step toward a matching plan in this specialty.

The present policies, and changes therein, of the American Boards of Internal Medicine, Obstetrics and Gynecology, Pediatrics, and Surgery were then described. These can, of course, all be found in the various Board regulations.

Several papers were then presented regarding the governance of medical schools today. It was felt that governance was not adequate to meet present and future needs because of the increasing complexity of the modern medical school. This complexity stems from several factors: 1. The explosive growth of medical schools, both in numbers of schools and numbers of students; 2. The vast change in medical schools by the proliferation of research programs; 3. The new programs in medical care; and 4. The diversity of sources of funds now available to the schools. Once existing as a place to teach medical students, the medical school has now become "big business."

The hierarchy of governance often starts with University Trustees, then the President, the Provost, and, finally, the Dean, whose job is becoming ever more difficult and whose role in governance seems to be getting smaller. In some universities, a Vice-President for Medical Affairs has been appointed, a sort of super-Dean, it seems. Department Chairman are becoming increasingly autonomous because of the outside funds in their possession. Dollars represent power, and these funds, of course, increase the responsibility to outside sources of income.

It was pointed out that the most influential role a University President plays in the Medical School is in the picking of a strong Dean. Although a Vice-President may relieve the President of some of his duties, he doesn't relieve the Dean of his basic duties and obligations, which include responsibility for the budget, assignment of space to different departments, appointing and discharging Department Chairmen, and so on. The importance of wise delegation of authority was stressed.

The faculty, also, has a place in the governance of the school. Ideas and programs must originate in the faculty, as must the development of the curricula, the admission and promotion of students, and questions of promotion and tenure among the faculty group.

Attention was then turned to "The Crisis in Medical Education."

The primary function of a medical school continues to be, as it always has been, the education of physicians. Research must play a large role, but the schools should not become merely research centers, nor should they be judged by research at the expense of medical education. Although research is an essential part of medical school, compulsory research is a contradiction in terms. There should be rewards for excellence in teaching, and educational functioning has almost no financial underpinning, as do research activities.

Emphasis was put on the great changes of the past twenty years, the doubling of a millenium of medical knowledge during that short period of time, and all the new clinical applications emanating from the tremendous strides in knowledge. The concept of service was discussed, and it was felt that this concept must be inculcated in every medical student and that service to the community must be regarded as an obligation of the modern medical school.

"Old doctrines and dogmas must be discarded." I feel many of us would disagree seriously with this loose statement but would agree that there are areas where change should take place and that perhaps "old dogmas and doctrines" should be supplemented by new knowledge without a change in what is basic in knowledge, tradition, and ethics in our ancient profession. It was argued that the "old system" of medical education had grown by accretion and was defective and wasteful from cost standpoint. Therefore, need is felt for reconstruction of medical education to make it shorter, better, and less costly.

Respectfully submitted,
Charles B. Cheney, M.D.

Doctor's Office

John P. Callan, M.D., announces the opening of an office for the practice of psychiatry at 3 MacDonough Place, Middletown.

Melvin J. Coolidge, M.D., announces the opening of an office for the practice of dermatology at the Columbia Towers Medical Building, 5 Ridgefield Avenue, Bridgeport.

Robert E. Hentschel, M.D., announces the opening of an office for the practice of surgery at 2660 Main Street, Bridgeport.

Paul V. DiGrazia, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 230 Danbury Road, Ridgefield.

Public Relations Notes

Why Infant Mortality is High

The high rate of infant mortality in America is a manifestation of the problem of the slums. It is not related to the adequacy of health care here, as some persons are insisting in seeking to justify the expansion of national health programs. These observations were made by the Chicago Tribune in an editorial published on April 6. The editorial follows.

Infant Mortality and The Slums

Chicago's figures on infant mortality, as tabulated in our recent news stories on the city's health problems, do not make pleasant reading. Nationally, the number of deaths per 1,000 births, during the first year of life, was 22.8 last year; for Chicago as a whole, the figure was 29.4; and for Chicago nonwhites it was 48.1.

There are many countries, of course, where high infant mortality does indicate generally poor conditions of medicine and sanitation and is thus chiefly a health problem. But the United States can be proud of its medical progress. As the figures show, and as Mr. Johnson acknowledged, the problem of infant mortality is concentrated among nonwhites in the big city slums.

Sweden owes its good fortune not so much to good medicine as to the relative absence of slums. As for this country, there are many explanations for the slums—industrial, educational, racial, and the government's own welfare policies—but medicine is not one of them.

To treat infant mortality as justification for a new national health program is therefore like dunking a child in iodine to sterilize a bruised leg. The problem is not with the health of America; it is simply another manifestation of the problems of the slums. Much as some bureaucrats might like to extend their domain to include a nation-wide, cradle-to-hot-rod program of child health, this is not the solution. It would merely divert attention from areas where it is needed to areas where it is not.

It is going to be hard enough to find effective and realistic remedies for the city slums, and the most effective ones will probably involve education and jobs. Health services will figure only as stopgap measures. The medical problems of the slums will go away when the social and economic problems of the slums go away, and not before, no matter what the government does or doesn't do about child health.

Medicare's Good and Bad Points

A New Jersey physician, writing in a national publication, has come out with an endorsement of Medicare—but with reservations. David Jay Scott, M.D., of Asbury Park, said the program is making high quality medical care available for the first time to many elderly persons unable previously to afford it.

Dr. Scott offered his assessment of the Medicare program in the February 24 issue of the Saturday Evening Post.

"The average elderly person is now getting a level of care that previously was available only to the rich," he wrote. "There are definite signs that Medicare is helping to improve the entire standard of health in the United States," Dr. Scott said, adding that increased medical attention among the elderly has helped uncover many undiagnosed diabetics and helped prevent strokes and heart attacks in those over 65.

"Generally the law has been a financial lifesaver not only for the patients but also for their families," according to Dr. Scott. And contrary to predictions, he said the Title XVIII Program has not hurt ward service teaching programs, since ward beds are filled by many non-Medicare patients.

These are the major benefits of Medicare, the New Jersey internist stated. What are its deficiencies? "First, there is the distinct threat of Government control—laymen making judgments on medical issues, price-fixing, an unbending bureaucracy—which would inevitably lead to the decay of American medicine.

"Secondly, Government's foot in the door can destroy a cherished tradition: the doctor-patient relationship. It is not generally appreciated, but when a patient signs a Medicare form, he is authorizing release of all information to those persons who will act on it. Many things are between doctor and patient and are not for public scrutiny. The patient loses this right of privacy with Medicare.

"The third deficiency is the possibility of overuse of Medicare by the patient. The hypochondriac threat hasn't developed yet, but if it does, there is nothing in the law that can curb it. A patient, for example, can go to 50 different doctors for the same inconsequential complaint.

"So Medicare dangles somewhere between heaven and hell (hell meaning socialization, to the medical profession). My own feeling is that we'll never be consigned to the demons."

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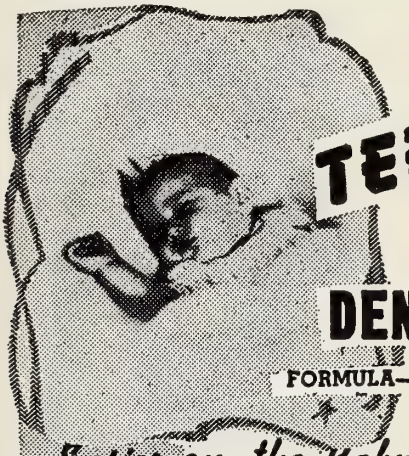

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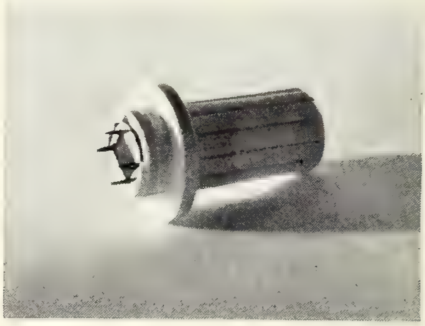

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MEETINGS

CANCER

May 8 **1:30-4:30 P.M.**

Current Concepts in Management or Oral Cancer

Peters-Darrow Conference Room
Yale-New Haven Medical Center

Advance registration necessary; fee $5.00

Contact: Office of Postgraduate Education, Yale University School of Medicine, 333 Cedar Street, New Haven, Conn. Phone: 562-1161 Ext. 864

May 16 **All Day**

Quality of Survival of the Cancer Patient

Hotel America, Hartford

Sponsors: Connecticut Division, American Cancer Society; American College of Surgeons; Vocational Rehabilitation Branch, U.S. Department of Health, Education and Welfare

Description: Discussion of the problems of rehabilitation of the colostomy, mastectomy, and laryngectomy patient; discussion of the cosmetic defects resulting from head and neck surgery. Speakers, Milton Edgerton, M.D., Johns Hopkins; Richard Jessie, M.D. Anderson Hospital; Maus Stearns, M.D., Memorial Hospital of Cancer & Allied Disease; R. B. Turnbull, M.D., Cleveland Clinic Foundation. Registration at 9:00 a.m., medical sessions, 9:30-11:30 a.m. and 1:00-5:00 p.m.; dinner meeting at 7:30 p.m.

Registration (free of charge) limited by invitation to members of selected medical groups.

Contact: Paul G. Kuehn, M.D., 85 Jefferson Street, Hartford; Phone 524-5939

May 22 **1:30-4:30 P.M.**

Current Concepts in Management of Laryngeal Cancer

Peters-Darrow Conference Room
Yale-New Haven Medical Center

Advance registration necessary; fee $5.00.

Contact: Office of Postgraduate Education, Yale University School of Medicine, 333 Cedar Street, New Haven, Conn. Phone: 562-1161 Ext. 864

MEDICINE

May 9 **10:00 A.M.**

Tuberculosis Control and Eradication in Connecticut

Holiday Inn, Meriden

Sponsored by the Connecticut Thoracic Society and the Connecticut Tuberculosis and Health Association

Open to all physicians; no registration fee

Contact: Nicholas D. D'Esopo, M.D., West Haven Veterans Hospital; Phone 932-2561

May 22 **10:00 A.M.-4:00 P.M.**

Symposium on Birth Defects, Prevention and Management

Main Auditorium, University of Connecticut Southeast Branch, Avery Point, Groton

Sponsored by the Connecticut Chapter, National Foundation—March of Dimes

Registration fee: $5.00

Contact: Mrs. Morton Katz, New Haven County Chapter, March of Dimes. Phone 787-7459

June 5 **10:00 A.M.-4:30 P.M.**

Physicians Workshop on Sex Education

Park Plaza Hotel, New Haven

Arranged by the Connecticut State Medical Society's Public Relations Division, Committee on Public Health, and Subcommittee on School Health. Financial participation by Ortho Pharmaceutical Corporation.

Workshop Topics: Sex Education in the Physician's Office, including the Physician's Attitude on Sex; Marriage Counseling; How To Counsel Teenagers; Sex Education in School Health Programs and Sex and Family Living Education for Adults; Human Sexuality, Including the Changing Role of Women.

No registration fee. For Advance registration contact Public Relations Department, Society Headquarters

June 10-14

Basic Principles in Internal Medicine—1968

Sponsored by the American College of Physicians

Purpose: To present the current understanding and treatment of diseases encountered by the practicing internist; the pathophysiologic derangements and their therapeutic implications will be discussed as well as newer diagnostic techniques.

Courses: Infectious Diseases, Endocrinology, Hematology, Nephrology and Hypertension, Cardiovascular Disease, Pulmonary Disease, Gastroenterology.

Fees: A.C.P. Members $60; nonmembers $100

Contact: Edward C. Rosenow, M.D., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia, Pa. 19104

PEDIATRICS

Cardiovascular Surgery

May 15 **9:30 A.M.-4:30 P.M.**

Mary S. Harkness Auditorium

Yale University School of Medicine

Description: The postgraduate program is designed to provide the practicing physician with information on emergency problems in the fields of pediatrics and cardiovascular surgery. It should be of value to physicians in family practice, pediatrics, obstetrics, and cardiovascular surgery. Speakers: Visiting Faculty, Denton A. Cooley, M.D., Professor of Surgery, Baylor University School of Medicine; William Rashkind, M.D., Associate Professor of Pediatrics, University of Pennsylvania School of Medicine; William T. Mustard, M.D., Associate Professor of Surgery, University of Toronto. Yale Faculty, Norman S. Talner, M.D., Associate Professor of Pediatrics; Marie J. Browne, M.D., Associate Professor of Pediatrics; S. David Rockoff, M.D., Associate Professor of Radiology; H. C. Stansel, Jr., Assistant Professor of Surgery.

Credit: This conference is approved for six hours credit by the Connecticut Academy of General Practice

Registration fee and tuition $25.00, luncheon included (interns and residents may register without charge)

Contact: Office of Postgraduate Education, Yale University School of Medicine, 333 Cedar Street, New Haven, Conn. Phone: 562-1161 Ext. 864

GENERAL

Hartford Hospital
Saturday Mornings **11:00 A.M.**

May 18

Compensatory Renal Hypertrophy

Speaker: Bernard Lytton, M.D., Professor of Urology, Yale University School of Medicine

May 25

Clinical Interprepation of the Pediatric Electroencephalogram

Speaker: Peter H. Berman, M.D., Department of Pediatric Neurology, New York University School of Medicine.

June 16-20

Conference of the Association of Food and Drug Officers of the United States (72nd Annual)

Hartford-Hilton Hotel

Contact: Eaton E. Smith, Division Chief, Connecticut Department of Consumer Protection, State Office Building, Hartford

NATIONAL MEETINGS

May 15

American Society for Gastrointestinal Endoscopy
Bellevue-Stratford, Philadelphia

May 13-16

American Urological Association
Fontainebleau Hotel, Miami Beach

May 13-17

American Psychiatric Association
War Memorial Auditorium, Boston

May 15-18

Neurosurgical Society of America
Mark Hopkins, San Francisco

May 19-23

American Thoracic Society
Rice Hotel, Houston

May 27-29

American Ophthalmological Society
Homestead, Hot Springs, Virginia

BOOK REVIEWS

SYMPOSIUM ON CORONARY HEART DISEASE. (Second Edition—Revised) American Heart Association Monograph Number Two. Edited by Herrman L. Blumgart, M.D. American Heart Association, Inc., 44 East 23rd Street, New York, New York, 10010. 161 pp. $3.00.

Reviewed by: LOUIS H. NAHUM

The first edition was published six years ago, however, the present monograph is virtually a new presentation. The contributors are the who's who in the field of cardiology and have discussed every aspect as the knowledge of coronary heart disease stands today even including a fine review by Howard B. Sprague on legal aspects of coronary disease and a delightful first paper by Paul Dudley White.

Each subject is authoritatively treated, is up to date and is followed by an extensive bibliography. Obviously a subject as large as coronary heart disease cannot be covered in such a few pages and the papers are more in the nature of a summary in which different points of view must perforce be considered. Nevertheless, the reader is left with the satisfaction that what is known is here and what is not known is also explicitly stated.

The fact that in a short time of six years, chapters have disappeared, because they are no longer of current interest, shows how rapidly our knowledge grows in this area and how important it is for us to keep this little paperback for reference on the newest ideas, thoughts and practices in this vital field. Whether you have a special interest in genetics, diet hormones, exercise, arteriography, anticoagulants, thrombolytic therapy, treatment, surgical and medical, comprehensive care of the coronary patient, it is all here. It is indispensable for the student, practitioner and cardiologist.

THIAMINE DEFICIENCY: Biochemical Lesions and Their Clinical Significance. Ciba Foundation, Study Group No. 28. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1967. 163 pp. with 46 illustrations.

Reviewed by HERBERT LEVINE

This monograph, subtitled "Biochemical Lesions and their Clinical Significance", reports the proceedings of a conference held in London on Nov. 10-11, 1966, honoring Sir Rudolph Peters of Cambridge, who also acted as chairman. The first three papers review the evidence from animal experiments that thiamine deficiency impairs the pyruvate oxidase system in the brain and other nerve tissue. Lowered blood pyruvate levels are nor per se a reliable test for thiamine deficiency in patients, however, since many other mechanisms may be involved. Certain analogues of thiamine act as antagonists to its action, and experiments with these have helped to show that thiamine pyrophosphate is the active form of the vitamin. Another series of papers based on animal experiments describes diminutions in transketolase and pyruvate decarboxylase in the nervous tissues of thiamine-deficient rats, but the relationship of these enzyme inhibitions to the pathogenesis of the central nervous system manifestations of thiamine deficiency in human patients is unclear.

There is one clinical paper describing some features of beri-beri and Wernicke's encephalopathy in humans, but this is the only real concession to the "Clinical Significance" mentioned in the subtitle.

This book has nothing to offer the practicing physician, but will be of interest to the biochemist as a description of experimental work on the relation of thiamine to various enzyme systems in nervous tissue.

DIABETES MELLITUS: Diagnosis And Treatment, Volume II. Edited by George J. Hamwi, M.D. and T. S. Danowski M.D. American Diabetes Association, Inc., New York, 1967. 250 pp. $2.50.

Reviewed by: PAUL H. LAVIETES

The first volume of this series was very useful. The second is equally so. It is somewhat longer than the first, reflecting the great increase in clinical investigation in diabetes in the past few years and in the many areas in which progress has occurred. The appraisals of various subjects which comprise the book continue to be those of the authors selected by the editors and are not a consensus. The reviewer believes that this is fitting, especially since there are so many areas in which accumulated experience has not led to indisputable answers. This is particularly true of the relationship of the metabolic disturbances to the complications of the disease, but also to genetics, objectives of therapy, diet, etc. It is thus very useful to have succinctly presented points of view by recognized experts who are cognizant of the work of others and who present good limited bibliographies.

An excellent Pathophysiology of Diabetes is presented by Dr. George F. Cahill, Jr., and there are interesting chapters on Epidemiology by Dr. Max Miller and Peter H. Bennett, Genetics by Dr. Arthur G. Steinberg, and Vascular Disease and Diabetes by Dr. J. M. B. Bloodworth, Jr. But most of the book is devoted to problems of direct clinical significance. This book is a must, not only for specialists in diabetes but also for all practitioners.

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The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the Journal (listing name and initials of author, title of article, journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

ILLUSTRATIONS

Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration as well as typed on a separate sheet. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. Connnecticut Medicine will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

NEWS

Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

ADVERTISING

All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by Connecticut Medicine.

Material other than original articles should be received not later than the 10th of the month PRECEDING date of issue.

REPRINTS

Reprint orders should be returned at once as the type will be destroyed immediately following publication of the manuscript. The Journal does not stock reprints of the articles published. Requests for individual reprints should be sent to the author.

Communications should be addressed to Connecticut Medicine, 160 St. Ronan Street, New Haven, Conn., 06511 Telephone 865-0587.

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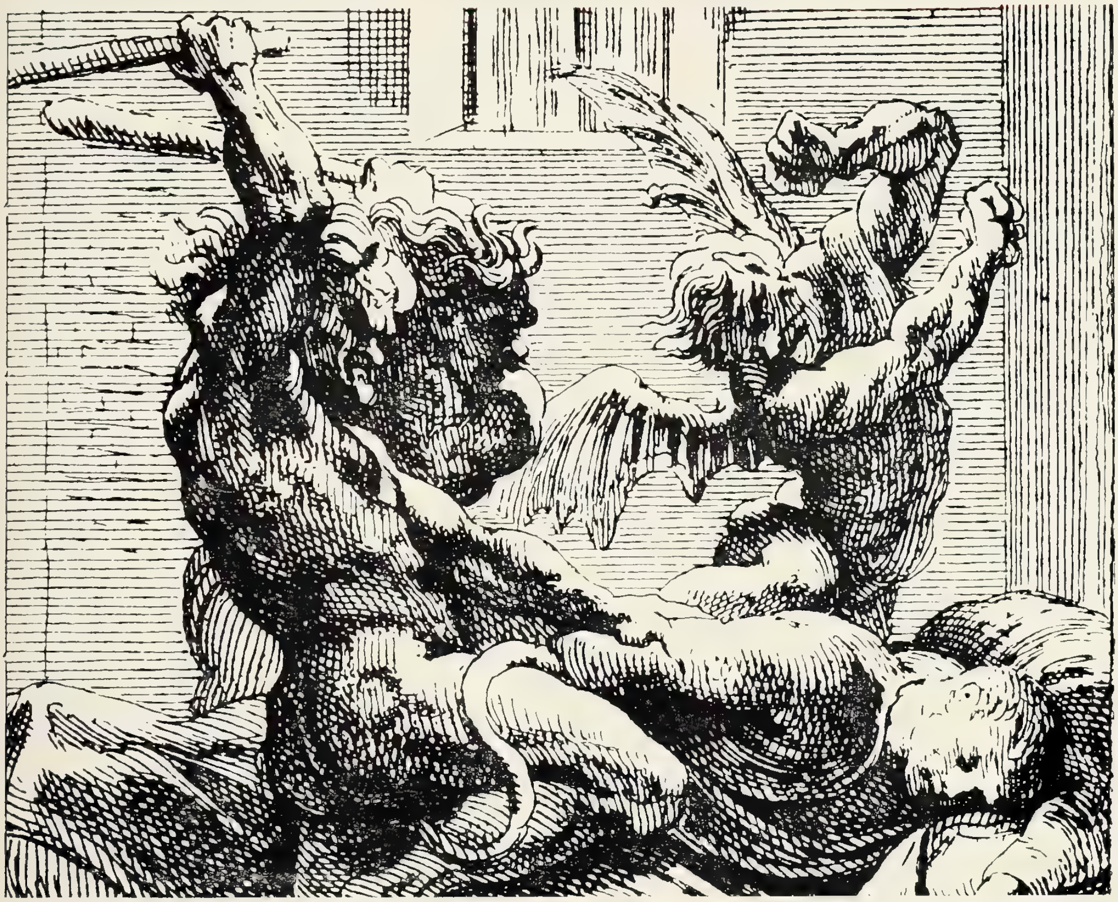
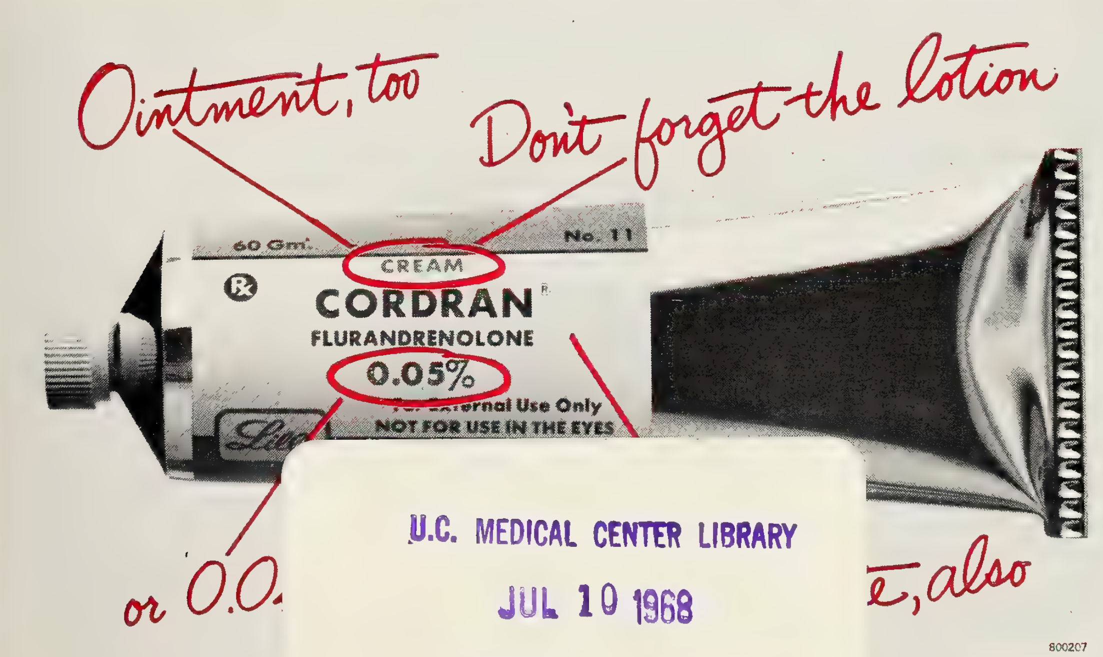


Man Tormented by Dreams—*Science*, March 1968

Melvin Lewis, M.D., *Guest Editor*



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Connecticut Medicine

JUNE, 1968
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CLINICAL ASPECTS OF THE PSYCHOLOGICAL DEVELOPMENT OF THE CHILD: I.

Melvin Lewis, M.D., *Guest Editor*

(This is the first of a two-part series)

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Connecticut Medicine

editorials

Genetic Betterment Through Germinal Choice: A Dream

It is now well known that human spermatoza can be kept deep frozen at the temperature of liquid nitrogen without deterioration during prolonged storage even though the process of freezing and thawing still incapacitates for fertilization a minority of them. The addition of glycerin and probably still better dimethylsulfoxide considerably reduces this undesired effect. At several places in this country and in at least one abroad, banks of frozen sperm are already being kept. The infants from the deep frozen sperm have been comparable in their normality with those from unfrozen unmanipulated sperm. So far there has been no attempt to procure for any of these banks the semen of donors who are outstanding.[1]

Research is badly needed concerning ways of "stretching" the amount of use possible for a given sample since suitable diluents long known for domestic animals have not yet been found for man. Nor have ways been found of reliably fertilizing a human egg by sperm in-vitro since some kind of sperm "capacitation" is needed beforehand which normally occurs in the fallopian tubes. Another need is to find out how immature germ cells that could of course be kept deep frozen like other tissues can be caused to develop into normal spermatozoa in-vitro. Such a discovery would make possible the unlimited use of a given sample of immature germ cells.

This knowledge is important because there are increasingly large numbers of couples who were suffering from sterility in the husband that would be eager to avail themselves if means of having one or more children derived on the male side from someone they both held in deepest regard as a person physically by no means inferior while morally and mentally outstanding. At present there are perhaps 10,000 children a year produced in this country by artificial insemination with semen from donors chosen by the physician. He however does not select the semen according to such standards and he keeps their identity secret from everyone including the couple itself. Well endowed children would be far more desired if the couples were allowed to exercise the deciding voice in the choice of the genetic father after seeing the records of a sperm bank with a wide range of possible germinal choices. The couples could receive counselling concerning the germinal material available and be able to judge which of them have shown more of the traits preferred by the couples themselves of children whom they themselves want.

To have openness of choice regarding donors it would be desirable that the semen to be used had been stored preferably for decades after the donor's decease, to avoid possible entanglements between him and the recipient couple. It would also allow perspectives on the donors' phenotypically expressed merits and their genetic liability in passing these along. This kind of information would be invaluable in making of choices. Of course couples would be counselled beforehand that genetic segregation and environmental influences do not allow the results of reproduction to be predicted, and that their germinal choice only weights the results in their favor. The counsellors probably would point out that outstandingly good performance in an offspring has almost always required a combination of both favorable environment and favorable heredity. The parents would be counselled that in heredity the child stands on the average halfway between the means of its two genetic parents.

As the results, so favorable on the whole, of the relatively few first trials gradually become known even more couples might wish to follow these pioneer's example. Is this not the way customs start? Previous taboos against the practice might dwindle. In their place a new atmosphere of hope would emerge, hope both for the rewarding results likely to accrue to the couples themselves and hope among them and others for mankind in general. At last human resources even on the genetic side woul begin to be enhanced at an accelerating pace. Despite differences in choice among couples they doubless would wish and should be guided to include some of the more special gifts or predilections such as cooperative dispositions, general intelligence and artistic creativity. The prospective parents would doubtless wish to consider physical traits also such as longevity, late senility, vigor, agility, good automatic regulation and beauty. While no one possesses all these mental and physical endowments a choice could be made by the couple which while largely consistent with the counsel also best fits the couple's ideal.

In getting such a project started it is of the utmost importance that rigorous precautions be taken to ensure that the persons in the group or groups undertaking it genuinely favor what they consider genetic improvement and of course all agreed on the major value of the traits such as the physical and mental traits mentioned above. The group of prime movers must, to start with, be small, carefully chosen and guided by rules that maximally safeguard their future observance of this interpretation of social values. They should have as participants not only persons specialized in genetics, in the physiology of reproduction in its theoretical and medical aspects in psychology and social sciences. There should also be representatives from the field of values and other truly humanistic fields. Muller who has had this dream of human betterment through germinal choice, tells us he has had approval of these ideas from representatives of all religions. Clearly unusual vigilance will be indispensable from keeping the aims of the genetic betterment group from becoming perverted.

With changing mores regarding germinal choice these services would eventually open up much more possibilities of choice to all couples. A preliminary choosing of donors as occurs now could become largely unnecessary. But all the more necessary would be the adoption of means of ensuring that the counsellors and those engaged in choosing germinal material for their families recognized and truly understood the major aims of genetic betterment of the human race. The measures mentioned here are much closer to realization than those of applied gene knowledge of the traditional kind and ever so much closer than those of "genetic surgery"—replacing a bad gene with a good one.

The geneticists who are concerned with man should see to it as a part of their own responsibility not only to enlighten the public but also to promote in the meantime, the collection, documentation and storage of exemplary germinal material. This should be that of men who best represent the major aims of enlightened civilization, such as cooperativeness, more creative and generalized intelligence, fine physical endowment.

On the whole physicians especially those concerned with reproduction and the genital organs, counselling in genetics and avoidance of harmful genes would be important to have as participants in inseminations carried out under the germinal choice project. At present they are hard to find but the work of getting the project going should be undertaken as soon as possible and both medical and legal aid will eventually be forthcoming. There will of course be difficulties but man has gone from height to height and he is now in a position if only he will to transcend himself intentionally and thereby proceed to heights yet unimagined. Our reward will be that of helping man to gain the highest freedom possible to to finding endless worlds both outside and inside himself and the privilege of engaging in endless creation.

L.H.N.

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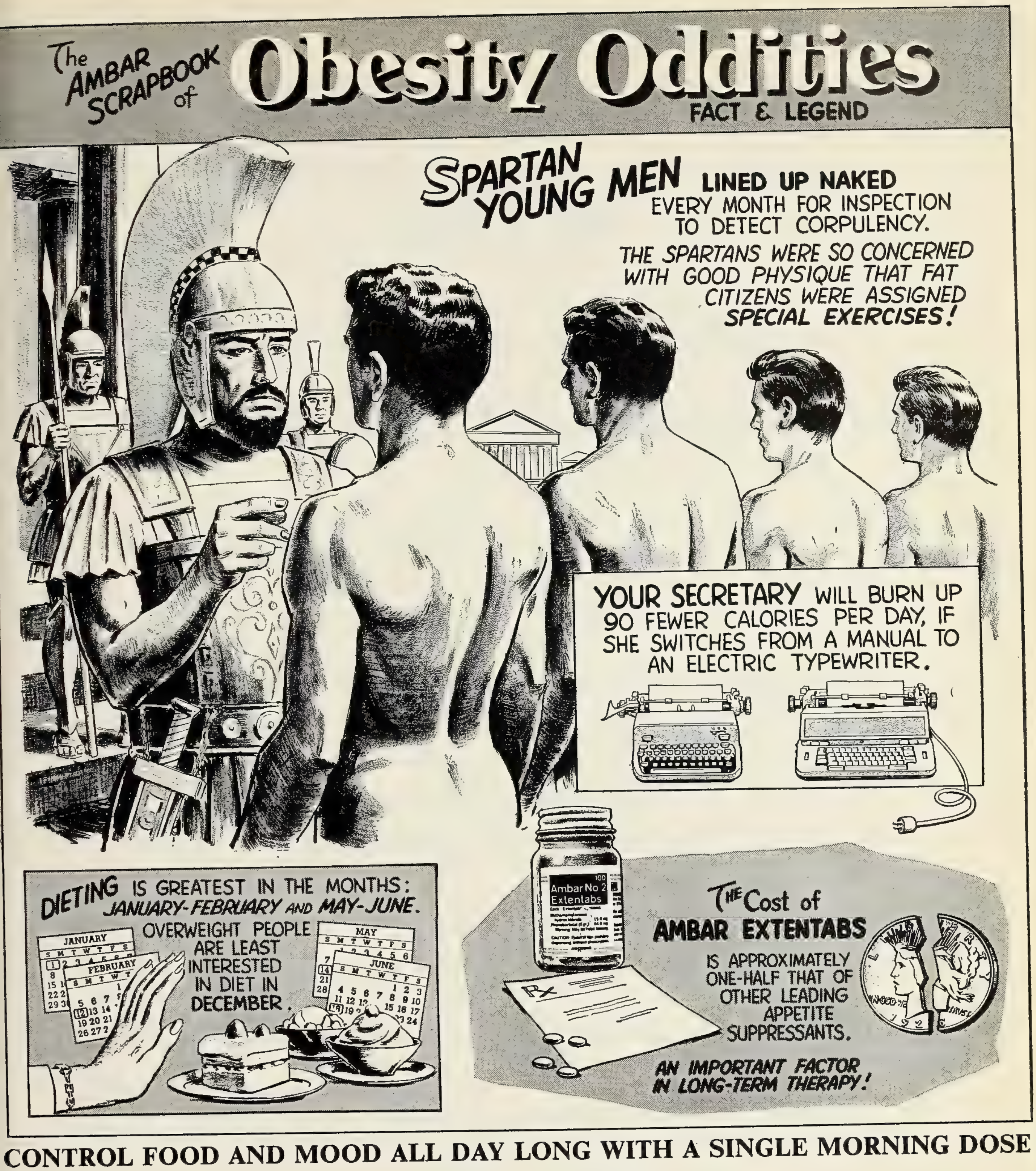
Disorders Of Arousal From Non-REM Sleep

Nocturnal enuresis, somnambulism, the sleep terror and the nightmare are important medical as well as social problems. The social impact can be appreciated from the extent to which they appear in the literature of various cultures. (Lady Macbeth's sleepwalking and the nightmares of Dante's Souls in Purgatory). These pose medical problems because of their frequency, their unresponsiveness to treatment and their similarity, in certain respects, to other more dangerous sleep disorders, such as nocturnal epileptic seizures and possibly the occasional death during sleep from an anginal seizure. Recent studies have helped clarify their pathogenesis.

Nocturnal enuresis is a common symptom in children and young adults. It has been reported in 10-15 per cent for nervous children, 30 per cent for institutionalized children, 24 per cent for naval recruits discharged on psychiatric grounds. The subject apparently asleep at the time of enuresis is difficult to arouse, is confused, disoriented even to the extent of not knowing the bed is wet and completely unable to recall any dreams.

In a typical attack of somnambulism or sleepwalking, the individual sits up quietly generally an hour or two after falling asleep, gets out of bed and moves about in a confused and clumsy manner. Soon his behavior becomes more complex and co-ordinated. He may avoid objects, dust tables, go to the bathroom or utter usually incomprehensible phrases. It is difficult to attract his attention. If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left alone he will go back to bed. It is very difficult to awaken him and when awakened he has no recollection of dreaming.

The sleep terror or pavor nocturnus attack of children is very different. The child abruptly sits up in bed and screams. He appears to be staring wild-eyed at some imaginary object. His face is covered with perspiration, his breathing is labored. Consoling has no effect, dream recall is rare and fragmentary and when recalled resemble daytime fantasies. The following morning the child has no recollection of the episode. These three disorders may be exhibited by a single subject at different times. All may appear in the family history. Of enuretic naval recruits, 34 per cent have a personal history and 25 per cent have a family history of sleepwalking. They may also be combined in a single attack, a sleep terror or enuretic episode being followed for example by prolonged somnambulism.

The nightmare or incubus of adults[1] has received particular attention over the centuries. During an attack the adult suddenly cries out in his sleep and shows all the signs of intense anxiety: sweating, a fixed facial expression, dilated pupils, difficulty in breathing. The anxiety is believed by many to be the most intense ever experienced by man. Well structured dream activity is rare, in contrast to the terrifying dream (see cover) which contains complex imagery, remains a sequence in time and is not accompanied by respiratory oppression. Reports of apparent dreaming are usually poor descriptions of oppressive situations such as being locked up in a tomb or having rocks piled on one's chest. There is no recall the following morning.[2] Subjects typically show intense daytime anxiety.

Freud[3] believed that both the incubus attack and the night terror of children express "repressed sexual impulses." The amnesia following all four attacks has often been considered as a result of "repression." More generally, however, they have been interpreted as due to dream activity despite the infrequency of dream recall. Recently the "dream hypothesis" of the pathogenesis of the sleep disorders has become verifiable because true dreaming has been shown to occur in association with a recurring and distinct physiological state, with manifestation of rapid eye movements—REM— a characteristic electroencephalogram and peripheral muscular atonia, together with good recall.

With these tools Broughton[4] has reported his results in subjects with the sleep disorders. He was therefore able to determine whether the sleep disorders occur during the dream state, and found that they do not. He then asked himself the question as to when they do occur, to what extent some or all of the symptoms of these apparently "psychological" disorders might be explicable by physiological factors associated with changes in the wakingsleep cycles. If there are neurophysiological mechanisms, to what extent do they underlie the common physiological correlates of the disorders? How relevant are they in explaining the symptoms of the attacks? To what extent, if any, is the attack pattern in a given individual determined by preceding physiological rather than psychological vents? Finally is the question of what might be the possible relationships of the attacks to various types of mental activity?

Broughton's conclusions from his careful studies of these sleep disorders permit definite answers to some of the questions he posed. First of all it became clear that the sleep disorders occur preferentially during arousal from non-REM sleep and are virtually never associated with the dreaming state. There exists physiological differences between these normal subjects of a type that predisposes the individual to a particular attack pattern and these are present throughout the night. The episode in the case of enuresis which he studied most intensively, usually began with body movement associated with increased muscular tone, tachycardia, or apnea during beginning arousal.

There were a number of features common to all four sleep disorders. There was a confusional period that follows non-dreaming sleep related to alterations in cerebral reactivity at least of the visual system. The symptoms which distinguish the individual attack types, that is micturition, prolonged confusional changes which are present throughout sleep but become markedly accentuated during arousal from non-dreaming sleep. Such changes may in some way be related to diurnal psychic conflicts. Thus far it has not proved possible to demonstrate causal psychological activity just preceding the attacks.

There are however predisposing physiological changes both during the day and night such as automatic functions involved in bladder emptying based upon the activity of the autonomic nervous system, such as heightened bladder tone and cardiac acceleration, disturbances of breathing, peripheral expressions of anxiety. This is perhaps why it is that efforts to cure the disorders at the moment of their occurrence, by conditioning pro-

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cedures (nocturnal enuresis) have been far from satisfactory.

Broughton stresses the point that the attacks are best considered disorders of arousal which sets the stage for these attacks, and that the arousal episode from non-dreaming sleep is a normal cyclic event. Indeed it is the most intense recurrent arousal that an individual regularly experiences. This is in contrast to arousal from dreaming sleep which is usually smooth and non-violent.

We are now at the threshold of fruitful possibilities for future research. We need more detailed studies of those physiological changes that predispose individuals to certain types of attacks when they undergo intense arousal or stress. Perhaps this type of information could offer a method for reversing these changes by psychological means as Freud's work suggests, or by pharmacologic means. The characteristics of the process of cyclic arousal from non-dreaming sleep both physiological and psychological will be awaited with great interest.

L.H.N.

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Cervical Venous Hum Or Bruit du Diable

If the physician listens in the neck above the mid-clavicle he may hear a continuous roaring or machinery-like sound, louder in diastole, increased by inspiration and easily obliterated by light digital compression of the internal jugular vein or with the Valsalva maneuver. This sound has been termed cervical venous hum or bruit du diable. The sound is best heard with the patient in the sitting position using light pressure with the bell of the stethoscope in the supraclavicular area just lateral to the clavicular attachment of the sternocleidomastoid muscle. It is more readily heard when the patient is upright often better on the right side and tends to disappear in the recumbent position. This is the reason why physicians who listen to the patient in the prone position may miss its presence.

To elicit the murmur the right hand of the examiner should place the bell of the stethoscope over the right supraclavicular area while the left hand grasps the patient's chin from behind. From this position he can allow the head to rest on the elbow curve thereby permitting all the neck muscles to relax. He can then move the chin superiorly and to the side thus placing the cervical veins on stretch. With this maneuver it is possible to change the pitch of the venous hum in a remarkable way. In addition it is possible to eliminate the murmur completely or alter it significantly by pressure of the fingers on the appropriate cervical veins.

The venous hum probably results from rapid downward flow through the artificially stenosed jugular vein. Although the murmur is continuous, often it is loudest in early diastole and may even envelop the second sound as in patent ductus arteriosus. In fact in may even be transmitted to the upper chest. It is thus easy to see how the murmur could then be confused with that of a patent ductus and in fact has occasionally been so confused. A correct diagnosis is easy to make if there is a change in the murmur when the position of the head is changed, if the murmur disappears with pressure over the jugular vein or the patient lies down.

The cervical venous hum is common in conditions associated with increased velocity of blood flow and high cardiac output. In the child the internal jugular vein is narrow and therefore velocity of blood in it is more rapid, especially when the child is sitting. The vein enlarges as the patient reaches maturity and this is why the velocity slows down and the murmur becomes less common in adults. Other conditions with increased velocity of blood flow are anemia, fever, beri-beri heart disease, thyrotoxicosis and pregnancy. Some patients with venous hums are variously diagnosed as due to arteriovenous fistula, pulmonary arteriovenous fistula or patent ductus when in fact it is due to a venous hum and can be made to disappear on pressure over the jugular.

Of particular importance is the finding of a venous hum with thyrotoxicosis. Most such patients have a venous hum and in fact absence of one makes the possibility of the presence of a toxic thyroid unlikely. The so-called thyroid bruit is often actually a venous hum. However, eliminating the venous hum by obstructing the jugular vein may still reveal a systolic murmur due to increased vasculature of the thyroid as well as a carotid artery origin for the murmur.

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Precautions: Use thiazides cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery, thiazides may reduce response to vasopressors, and increase response to tubocurarine. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia) in all patients. In hypokalemia (especially in digitalized patients) give supplemental potassium. In hypochloremic alkalosis, give supplemental chloride.

Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

Adverse Reactions: Thiazide reaction include blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, serum uric acid or blood sugar; anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, symtomatic gout, and pancreatitis. Cutaneous vasculitis in the elderly has been reported with other thiazides. Adverse effects with deserpidine are qualitatively similar to those with reserpine, but their incidence is lower. These include nasal stuffiness, abdominal cramps or diarrhea, nausea, headache, weight gain, reduced libido and potency, peptic ulcer aggravation, epistaxis, skin eruption, asthma in susceptible patients, electrolyte imbalance, excessive salivation, and a reversible Parkinson's syndrome. Excessive drowsiness, fatigue, weakness, and nightmares may signal mental depression. Thrombocytopenia, purpura, and a symptom manifested by dull sensorium, deafness, uveitis, glaucoma, and optic atrophy are rare allergic reactions to other rauwolfias. Hypotension from antihypertensive agents may precipitate angina attacks in susceptible individuals. Usually adverse reactions disappear when drug is withdrawn.

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Sensitivity to thiazides; severe renal disease (except nephrosis) or shutdown; severe hepatic disease; impending hepatic coma from thiazide-induced hypokalemia.

Warnings—Patients: 1. No other drugs (particularly "cold preparations" and antihistamines), cheese or alcohol without physician's consent. 2. Promptly report orthostatic symptoms, severe headache, other unusual symptoms. 3. Angina pectoris or coronary artery disease patients must not increase physical activity with improved anginal symptoms or well-being.

Physicians: 1. Use antihistamines, hypnotics, sedatives, tranquilizers and narcotics (meperidine contraindicated) cautiously in reduced doses. 2. Stop Eutron two or more weeks before elective surgery; in emergency surgery reduce premedication (narcotics, sedatives, analgesics, etc.) to 1/4 to 1/5; carefully adjust anesthetic dosage to patient response. 3. Use cautiously in advanced renal failure. 4. Pargyline may induce hypoglycemia. 5. Consider possible sensitivity reactions when a history of allergy or asthma is present. 6. If potassium is indicated, dietary supplement is recommended; enteric-coated potassium tablets may induce serious or fatal small bowel lesions (stenosis with or without ulceration), cause obstruction, hemorrhage, and perforation frequently requiring surgery; discontinue medication immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occurs; Eutron does not contain added potassium. 7. Possible systemic lupus erythematosus has been reported for thiazides.

Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804438R

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patients there is a communication of dilated tortuous arteries and veins without an intervening capillary bed, so that the cerebral blood flow is markedly increased with very rapid return flow through the jugular veins. Nevertheless in the 1000 such patients that Hardison[1] reviewed he found no mention of the presence of such a hum which was very pronounced in the two such patients he described in detail, The failure to record this murmur by other is not surprising since physicians rarely specifically listen for venous hums. However, cranial or orbital bruits have been noted but in such patients arteriovenous malformations were quite large.

The opposite, namely hearing a venous hum but not thinking of a possible origin in an intracranial vascular lesion is probably also true. Levine and Harvey[2] described a 36 year old woman with a chief complaint of a roaring noise in her head and who exhibited a loud venous hum which disappeared after jugular compression and the patient could state exactly when the "noise in her head" disappeared or returned. The noise was very great and was a great bother to the patient. Levine fashioned a "choker" around her neck which seemed to relieve her complaint. No study was made to determine whether the patient had an arteriovenous malformation inside the cranium.

Hardison's report of two such cases emphasizes the fact that a venous hum heard by either the patient or physician especially in the adult should lead the physician to consider all the abnormal states that might be associated with a venous hum including intracranial arteriovenous malformations

L.H.N.

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Using Both Sides Of Our Central Nervous System

The connection between the two cerebral hemispheres is provided by the great commissure of the brain the corpus callosum. Through it the ascending and descending pathways connecting the cord with the telencephalon are crossed. By this means the ascending sensory and descending motor impulses pass to the contralateral side of the body. An important evolutionary factor is seen in the crossing of optical pathways. The visual image on the retina is already inverted as a result of physical refraction of the lens. The complete decussation of visual fibers found in many animals allows visual impressions from the left to pass to the right hemisphere of the brain where it is rendered upright. Tactile and auditory senses also cross so that they can be integrated in one hemisphere. For the right hand to know what the left hand is doing there must also be connections between the two hemispheres.

Anatomically the two hemispheres are the same, we learn to talk with both hemispheres and we use both hands with equal dexterity in our childhood games. The great change comes beginning with school. Now one hand become the work hand and only one hand learns how to hold the pencil.[1] The baby language is superseded by the logical sharply defined written language so that the half of the brain which directs the writing hand also becomes the seat of the large vocabulary of the adult. The process by which language becomes consolidated in one hemisphere is a slow one which is probably not complete until about the tenth year of age. From this point on the subsequent development of the brain is dominated by one hemisphere. Thus the whole of the knowledge we accumulate at school concentrates in one hemisphere and all our manual dexterity usually in one hand.

Except for some ambidextrous people the left hand is clumsy in performing some task normally assigned to the dominant right hand. And so we are faced with the grotesque situation that only one of our two anatomically well developed cerebral hemispheres is fully utilized functionally. And so we witness catastrophic effects of a paralytic stroke in the dominant hemisphere which immediately deprives the victim of the use of his writing hand and of the faculty of speech. The non-dominant hemisphere though responsible for the contralateral side of the body cannot help us to perform an act of skill with the left hand. For normal use this hand is degraded to functioning like a vice merely serving to assist the dominant hand.

Nevertheless the left hand does learn what the right hand is doing by way of the connecting corpus callosum. This part of the brain develops relatively late in comparison with the other parts of the brain. By the fifth month of pregnancy axones of special cells of the cerebral cortex have left their own hemisphere to make contact with neurons in the other. The number of communicating fibers grows to incredible proportions amounting to almost 200 million in a five month old child. Each hemisphere becomes connected with the other at almost every point.

From recent experimental work on animals new facts have come to light. The corpus callosum permits for the exchange of new experiences and through it the left side can communicate to the right side what it learns. This was observed following section of the optic chiasm. Some animals are without preference for one extremity. In these the corpus callosum serves to connect the two hemispheres on an equal basis. We have already seen that in humans this equality is not maintained in strokes and also in surgical removal of one hemisphere to prevent severe generalized epilepsy.

It is surprising to see to what extent one hemisphere could assume charge of the motor and sensory function of the whole body. Brain damage when suffered in early childhood or at operation gives rise to spastic hemiplegia, but the patient was nevertheless able to move both sides of his body and interpret stimuli from the homolateral side quite well. This was new knowledge one hemisphere has access to both sides of the body. Animal experiments and examination of humans then showed that not all pyramidal fibers decussate but that some 15 to 20 per cent course to the same side and are utilized to perform coarse voluntary movement on that side. From such observations we are permitted to conclude that one hemisphere receives afferent sensory stimuli from both sides of the body and exerts a control of the motor function of both sides.

In emergency situations such as after hemispherectomy it is unequivocally clear that the remaining hemisphere performs a relatively high degree of motor and sensory integration on the same side which normally is controlled by the contralateral hemisphere. The patient is able to walk, to move all four extremities at will. He cannot execute fine finger movements on the contralateral side but he can adduct the thumb even when he has been affected by spastic paralysis from his early childhood until the time of operation. The patients exhibit an ordered mind, full power of expression and an urge to learn. One such patient took a lively interest in laboratory equipment and learned the technic of photography quite on his own accord. He carried out his occupation as a fitter of motor car accessories. There undoubtedly is a relatively large potential of one hemisphere and

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the corpus callosum helps the non-dominant hemisphere to learn. This faculty, however, diminishes with growing up, as witness the clinical experience with apoplexy on the dominant hemisphere.

How then can we exploit the potential quality of the hemispheres as a means of providing against the great intellectual loss which results from injury in the dominant hemisphere of the brain? Glees recommends systematic exercise of both hands, of doing everything which might favor learning in the other hemisphere that which supports the function of the corpus callosum. When one tries to recognize an object with the left non-dominant hand, the right hemisphere transmits via the corpus callosum. When one tries to recognize an object with the left non-dominant hand, the right hemisphere transmits via the corpus callosum its tactile characteristics for identification to the left hemisphere. Clearly a better arrangement would be for the non-dominant side too, to have such a store.

Here we have a fertile field for the Behaviorists to study intensively how we can utilize better our two hemispheres. We are endowed with them why not learn how best to use them.

L.H.N.

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Who Should Receive Mumps-Virus Vaccine?

Hilleman and his associates isolated mumps virus from a child and succeeded in attentuating the organism by passage in embryonated hen's eggs and then in chick embryo culture from which the vaccine was finally prepared. It was then evaluated in children for clinical reaction and protective efficiency against natural mumps in extensive studies carried out in the Haverford Springfield suburb of Philadelphia. The vaccine was shown to have a high level of efficiency without causing apparent clinical reactions.

In their present paper[1] data are presented relating to application of the vaccine in clinical practice. It was administered to 6,283 initially susceptible children and 163 adults including 132 males. They found no evident clinical reactions to the vaccine either in adults or children including infants. The protective efficiency shown on natural mumps challenge was of the order of 95 per cent and the protection was shown to last at least twenty months. The neutralizing antibody induced by the vaccine persisted for at least two years without substantial decline and the pattern closely resembled that for antibody persistence after naturally acquired mumps. The vaccine could be administered with live measles vaccine with satisfactory responses to both. It appeared, however, practical to delay vaccination to twelve months of age to permit loss of passively acquired antibody and to achieve maximal vaccine effectiveness.

All this suggests that this immunizing agent may possess nearly ideal qualities. But the question arises to whom should it be given and when. Those who believe it should be given to every child point to the personal discomfort, loss from productive effort and serious or even fatal aspects resulting from mumps-virus involvement of the brain, ovary, testis, auditory nerve or pancreas to justify application of a safe and effective live virus vaccine especially if it affords lasting immunity. The fact that the serum antibody assayed after vaccine administration range from as low as 15-25 per cent of the titre found after natural mumps-virus infection merely means that a technical problem of perhaps dosage administered remains to be resolved.

Others, however, are more cautious about mass mumps-virus vaccination. In the example of polio and measles, epidemiological data were available with which to evaluate and substantiate the significant toll in human life and potential exacted by the naturally occurring diseases. In the case of mumps we do not have comparable figures. For example we do not know how frequent central nervous system damage is observed, probably extremely infrequently. The feature of the disease that has been of most concern to fathers and physicians for centuries is orchitis which may develop in approximately 20 per cent of males who acquire the infection after puberty. This anxiety stems from fear of impotence and sterility sequelae that have been suspected to occur rarely if at all. Nevertheless, they generate great emotional concern.

One serious but very rare complication may be unilateral nerve deafness. There has not been enough accurate reporting of the illness with careful definition of its complications to make it possible to state definitely the frequency of any of these or other possible sequelae. Added to these specific uncertainties are others much discussed possible hazards (not demonstrated) of occult contaminating agents sensitization and even oncogenicity that may accompany the use of live virus vaccine.[2]

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If the disease to be prevented is serious, the speculative or extrapolated risks will have relatively less weight. If the disease is relatively benign then one would tend to give more weight to the possible hazards inherent in live virus vaccines and consider a conservative approach to the use of the vaccine rather than a mass program. In fact such conservative recommendations for present use of the vaccine have been adopted by the American Academy of Pediatrics Committee on the control of infectious disease[3] and Recommendation of the Public Health Service Advisory Committee on Immunization.[4]

They suggest that it be used for males approaching or past puberty who have not undergone natural mumps infection. Additionally they state that it might be indicated in certain institutional settings where an outbreak among a closed population could disrupt patterns of usual activity.

These recommendations are obviously limited because of absence of well controlled vaccine studies. When we succeed in acquiring reliable information on current morbidity of naturally occurring mumps and its possible complications, the recommendations may then be altered. In the meanwhile we urgently need answers to the more general problems involved in the use of immunizing agents live or inactivated and for this we must foster continuing research in the basic area of virology and immunology.

L.H.N.

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Soaps And Photosensitive Dermatitis

Tetradechlorsalycilanilide is an antimicrobial agent which had been added to soaps shortly before an outbreak of photosensitive dermatitis occurred in England about 1960. It was soon found to be the cause of the dermatitis and when subsequently this substance was removed from soaps in England no more such cases occurred. When it was used in this country in test-market areas it again caused photosensitive eruptions. Recently a related compound tribromosalycilanilide and two isomers have been added to soaps in the United States as antimicrobial agents and several cases of photosensitive dermatitis due to these substances were soon reported.

A recent report by Ison and Tucker[1] describes twelve additional patients with photosensitive eruptions due to halogenated salycilanilides in soaps. In these the diagnosis was confirmed by positive photopatch tests. In their report is also detailed a method of determining which of the halogenated salycilanilides are more likely to cause photosensitive dermatitis. This test-system uses an artificial light source especially designed to study the patients and this has offered a reliable simple method while also providing distinct advantages over pervious ones.

A photosensitive reaction typically appears as a sharply demarcated, moderately severe, acute and chronic eczematous dermatitis limited to the exposed parts of the body.[2] A combination of a chemical compound and ultraviolet light is required to produce the disease since neither alone will cause the photosensitive eruption. Systematically administered chemicals may also be photosensitizers and the clinical manifestations are similar to those from topical application. One must recall that contact dermatitis due to airborne or other external agents may resemble photosensitive eruptions and have to be differentiated from them. For this reason one needs two types of evidence to establish the diagnosis. First is a carefully taken history of all drugs and topical medications used and then photopatch testing to confirm the clinical diagnosis when a photosensitive dermatitis is due to topically applied agents. The twelve patients of Ison and Tucker used Lifeguard, Lifebouy or Zest soaps containing the halogenated salycilanilides and improved when the soaps were eliminated. Subsequently a flare-up of the dermatitis occurred in two patients when they tried the soaps again.

Since World War II a large number of oral drugs[3] have been marketed that magnify the ordinarily relatively harmless ultraviolet light to a destructive force producing unpleasant and in some instances disabling sensitivity. The drugs include the phenothiazine tranquilizers, antibacterial and antifungal agents (tetracyclines, sulfonamides and griseofulvin) hypoglycemic agents (sulphonureas)

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diuretics (chlorothiazides) and antihistamines (promethazine).

Since 1961, after the introduction of antimicrobial agents into common household toilet soaps and other topical preparations, contact photosensitivity has become an important medical problem. Reports such as that of Ison and Tucker have motivated the FDA to order removal of bithionol, a potent contact sensitizer, from at least seventy commercial preparations including shampoos, rinses, soaps and antiseptic creams.[4]

The specific wave lengths of light necessary for the initiation of this type of contact photodermatitis are in the long ultraviolet range, 320-400 mina meters. Then are the wave lengths usually associated with no known biologic reaction other than pigment darkening. Just how the light serves to trigger the reaction to halogenated salycilanildes is currently under study. In vitro findings have indicated a chemical alteration in the compound after ultraviolet exposure producing a homolytic cleavage of the carbon-halogen bond creating a highly active compound.[5] This unstable new compound can be reconstituted or can combine with numerous naturally occurring constituents of the skin including proteins. It has also been postulated that this newly formed protein—salycilanilide complex can act as a complete antigen unit and that contact photosensitivity is a form of delayed hypersensitivity similar to that of contact eczematous dermatitis.[6]

There is no doubt that photosensitivity is an alarming clinical problem, frightening and disabling to the patient and perplexing to the physician. Once the diagnosis of photosensitivity is suspected, Ison's procedure points the way to a definitive diagnosis. What is especially necessary, however, is for the soap industry carefully to screen all soap additives for their photosensitivity capacity before being added to soaps. Had this been done after the experience in Britain our population would have been spared the disabling photosensitivity resulting from the use of medicated soaps.

L.H.N.

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And Now The Hand Lotion

In 1967, Morse[1] described an outbreak of septicemia due to K. pneumoniae (serotype 18) resulting from the use of a heavily contaminated hand cream dispenser. The decanter bottle had been filled repeatedly with a variety of common skin lotions. The assumption was that it had become inadvertently contaminated. The finding called attention to the value of investigating hand lotions as a possible nosocomial hazard. Morse, et al's recent experience[2] involved a twenty-four year old woman hospitalized because of pulmonary emboli secondary to thrombophlebitis of the pelvic veins associated with early pregnancy. A venous catheter was inserted on the tenth hospital day. Cultures from the blood and from the removed venous catheter grew out non-chromogenic S. marescens. The patient was critically ill and recovery followed administration of chloramphenicol. A spontaneous miscarriage occurred during convalesence.

Infections due to S. marescens have been reported with increasing frequency. In fact, many reports describing the increased occurrence of Gram negative bacterial infection in hospitalized patients have appeared in the past few years. An annual analysis of positive blood cultures at the Saint Vincent's Hospital in Worcester[1] depicts a significant decrease during the past five years in the occurrence of septicemia due to Staphylococcus aureus and increase due to Gram negative bacteria particularly E coli, K. pneumoniae, enterobacter and S. marescens.

In view of their findings above of an outbreak of septicemia due to K. pneumoniae resulting from the use of a heavily contaminated hand cream dispenser, Morse and Schonbeck[2] have just reported the result of direct cultures of commercially available hand lotions from both opened and unopened bottles. From four of twenty-six brands examined they identified an array of Gram negative bacteria. One nationally distributed brand sampled from different retail outlets in two separate communities contained impure growth nonchromogenic S. marescens in a concentration ranging from 45,000-

460,000 organisms per ml. in nine previously unopened bottles.

The second nationally distributed brand is used exclusively in hospitals and is distributed to each patient on admission. Pseudomonas aeruginosa in an average concentration of 175,000 organisms per ml. was isolated from both opened and unopened bottles. The other two implicated brands are produced locally and are the only hospital distributed hand lotions used in two additional institutions. From one brand (Hospital B) Escherichia intermedia, P. aerogenosa, K. pneumoniae, Alcaligenes faecalis were isolated from all samples (opened and unopened) in a concentration ranging from 44,000 to 7,500,000 organisms per ml. This product is commercially manufactured and regionally distributed.

In addition to being used as a hand lotion it is issued to each patient at the time of admission to the hospital and used for skin massages and back rubs. From the fourth hospital (Hospital C) nonchromogenic S. marescens and A. faecalis were isolated from all opened and unopened bottle samples, in an average concentration of 445,000 organisms per ml. This product is manufactured by the hospital pharmacy and is distributed throughout the institution. It is also available commercially from the hospital pharmacy. The other twenty-two brands cultured were free from bacterial contamination. The only point is that only one or two bottles of these brands were sampled. Others might have been contaminated also.

It is obvious that hospitals should be alerted to the potential infection hazard from the use of contaminated hand lotions. Hand lotions as we all know are extensively used, especially within the hospital environment and the recognized increase in infections due to Gram negative bacteria may be related to the use of contaminated products. We will now need to have all hand lotions first checked for sterility and release only bacteria free preparations to the patients.

L.H.N.

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Conditioning For Health

It is true that exercise during the early stage of the atherosclerotic process in the coronary arteries may be of particular value in promoting the growth of collateral channels, then a program of exercise starting early enough and properly conducted might make other curative measure unnecessary in many cases. In addition the reduction of obesity and the hypercholesterolemia which could be affected by exercise could be expected to remove some of the risk factors we now recognize as contributing to the development of coronary artery disease. This points up a need for analyzing the concept "exercise" and to consider ways in which it could be made most effective as a prophylactic in coronary artery disease.

Exercise is a vague term actually. Different kinds of intensities and duration of exercise accomplish very different results. There is the moderate type of exercise particularly walking which should be pursued every day for at least one hour. This is essential for maintaining body weight especially in mesomorphic or mesomorphic–endomorphic types of individuals.[1] The limbering, coordinating and strengthening exercises, although useful in training young people, are types of exercise which are of probably less significance as far as health is concerned.

There is the constant physical vigorous labor extending over a whole day which, however, is obviously incompatible with employment of most Americans. However, we know that this type of work permits individuals to handle a diet high in saturated fats without the usual increase in serum cholesterol. It also appears to be beneficial in regard to elasticity and patency of the vessels of the heart and is associated with a lesser mortality from coronary heart disease.

Exercise which considerably increases the work of the heart if properly spaced will train the cardiovascular system. The intensity does not need to approach the maximum energy expenditure. Under such extreme conditions a portion of the energy breakdown comes from anerobic processes, leads to liberation of lactic acid into the blood and local liberation of kinins which tend to promote local vaso dilation.[2] It could be of immediate benefit to the cardiovascular system and is of special value to the athlete competing in sprint-type events. It is definitely not indicated for the middle-aged man in need of conditioning.

The nature of this relatively intense exercise is of little importance provided a large enough fraction of the total muscle mass is involved. The larger the muscle mass involved, the greater will be the heart response. Push-ups involve essentially the muscles of the arms and shoulders whereas running, rowing, and swimming involve most larger muscles. While it is desirable for a younger man still in good condition to build up his practice for exercise to a half hour daily with an expenditure of 500 k. calories, Swedish results show that three fifteen minute periods of intensive exercise a week, together with the daily hour of walking are sufficient to improve cardiovascular fitness to a considerable extent.[1]

These generalizations raise important questions about what practical advice we can give our patients. Various rules have been suggested in regards to conditioning. For example exercise should not be so violent as to cause a pulse rate over 110 after one minute of exercise. This is too general an advice in a situation which exists in this country where a person cannot easily be referred to a reconditioning center for basic measurements of performance on a treadmill or a bicycle ergometer. It appears that in Sweden bicycle ergometers are becoming common in factories and office buildings. These not only allow individuals to know their physical limitations at a given time, but also serve as a powerful incentive by measuring improvement in conditioning. They learn changes in their maximum performances and pulse rates for varying levels of energy expenditure.

Golf with vigorous walking and other competitive sports are both good exercise and promote mental relaxation because they require almost complete absorption and hence exclusion of the days worries but on a daily basis are often too difficult in practice. Running is cheap, requires no partner or equipment. At equal energy expenditure, the stress on the heart is less if the leg muscles rather than the arm muscles are used. This is especially applicable when dealing with middle-aged men out of condition. Early in the morning before breakfast is a good time for running particularly in suburan neighborhoods. However, it may be more convenient to do it at the end of the day and this is not harmful. In fact at this time the muscles will be somewhat "warmed up" by the normal activities of the day. Exercise before supper will usually decrease rather than increase appetite.

There are also psychological advantages of a "break" at the end of the day whether before supper or before going to bed. Also it is advisable often to tell a patient to exercise at a time when he will not be distracted from attention at home and be discouraged by inactive neighbors. Last but not least is the cardinal principle that conditioning should be gradual so that increase in physical activity is built on previous performance. In this way there will occur a steady improvement without excessive effort.

It is quite unfortunate that we do not have in this country the equivalent of the European reconditioning centers. West Germany has a number of such centers where tens of thousands of workers are reconditioned during periods of four to six weeks. These centers are operated by insurance companies as well as by big industrial enterprises. They will accept a man on recommendation of his insurance physician at insurance expense. The centers are operated by physical educators and under medical supervision. They present a systematic program of calisthenics and endurance exercises such as swimming, running, games and also health lectures. Significantly, the men selected for such programs are those judged to be "prone to heart disease."

The USSR has a program of much greater magnitude with five million persons going through such reconditioning centers. Other eastern European countries also have large scale programs of this type. We do not have such facilities in this country. This requires that internists and general physicians should be much more directive in regard to a patient's schedule of activity and we need particularly to give close periodic attention to our patient's cardiovascular function, to recognize the existence of risk factors and strive to remove them. We need also to know the patient's cardiovascular function before and after exercise.

Those of us who are concerned with the compelling problem of the prevention of heart disease need also make our voices heard with the planners of Regional Medical Program to the end that they will include the establishment of reconditioning centers in their plans for dealing with heart diseases. We need prevention fully as much as treatment if not more so.

L.H.N.

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Improving The Memory Function By Drugs

There is great interest in finding drugs that can improve memory function, both as tools for research and also for therapy. Two drugs have been known to improve memory function. Strychnine was early recognized as facilitative in maze learning. Later confirmation came also from effects on memory by picrotoxin. However neither of these drugs are useful in man because the effective dose is too near to the toxic level. The data obtained from these drugs was useful, however first because they indicated that memory could be improved by drugs and second that they could be used as a means of comparison with the effects of any new drug that might be applicable to improve memory in certain geriatric patients.

Irwin and Bennazizi, in a one trial learning procedure observed even greater effects with pentylenetetrazol (metrazol) in dosages that are commonly used to treat geriatric patients. It mattered not whether the oral administration preceded the initial experience or immediately followed it. The drug was orally administered in dosages of 1-30 mg/kg immediately after the first trial of overcoming a hurdle. A second trial came 30 minutes before or immediately after the first trial. The results showed clearly that memory retention was significantly improved by metrazol, the minimum effect being obtained from 3 mg/kg. With this dose which is 1/60 of the convulsive effect he obtained more marked improvement in memory than by picrotoxin or strychnine.

The question arose whether the results reflected short term memory retentions with its rapid decay or whether the drug caused consolidation of the memory trace for longer term storage and readout. If either strychnine or metrazol were administered before the one trial learning rather than after the first trial, the retention was greatly improved.

The dosage of metrazol was only 1/100 of its convulsing dose so that the improved learning could not be due to this type of activity. However it is the convulsant action of strychnine and picrotoxin that improves readout. The question therefore arises how they do this.

Eccles work informs us that the three agents differ significantly in their neurophysiological modes of action. Strychnine blocks the postsynaptic inhibitory pathways. Picrotoxin blocks presynaptic inhibition, while metrazol blocks neither forms of inhibition. The excitatory effect of metrazol on the nervous system seems rather to result from a decrease in neuronal recovery time without reference to inhibitory pathways. Nevertheless strychnine and picrotoxin by eliminating inhibition must also result in decreased time of neuronal recovery.

One could therefore accept the fact that whatever decreases time for neuronal recovery would lead to acceleration of neuronal and synaptic transmission throughout the nervous system. Perhaps effects of small doses of metrazol on improved memory may also be due to possible specific regional effects on the brain that remain unknown.

If pentylenetetrazol does improve memory functions in therapeutic doses it could be a boon to many geriatric patients. It is hoped that it will be a fore-runner to other perhaps more effective drugs and that the well staffed pharmaceutical industry will take this problem up from here.

L.H.N.

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Packed Red Cells

The indiscriminate transfusion of whole blood rather than selected components is no longer justified in the practice of medicine. Modern approaches to treatment make it mandatory that each patient be transfused only after careful evaluation indicates which of the many blood components can best serve him. In particular, the use of whole blood when only erythrocytes are required is a distinct hazard to many patients and an unjustifiable waste of valuable plasma components in others. *Almost all patients who need transfusion can be effectively treated with packed or sedimented red cells rather than whole blood.*

Packed cells should be used for treatment of all patients with chronic anemia. These persons need the oxygen carrying capacity of the erythrocytes, but are in no way benefited by the extra fluid or small amount of protein in the plasma. In the absence of acute and significant bleeding packed cells should be given when treating the anemia of cancer, leukemia, lymphoma, uremia, arthritis, chronic blood loss, prenicious anemia, lupus erythematosis, and all other chronic illness. The low hemoglobin or hematocrit value in such patients is partially a manifestation of their relatively increased plasma volume. In most cases nothing is gained by a further expansion of the plasma volume with whole blood, and not infrequently the infusion of extra *and unnecessary* plasma leads to heart failure. For all practical purposes acute significant hemorrhage is the only indication for whole blood in medical patients. The medical service should use packed cell transfusions *routinely* and prescribe whole blood only in those few instances when it is specifically required.

Packed cells are absolutely indicated when transfusing patients with actual or incipient heart failure. Here circulatory overloading is a serious complication of transfusion. Packed cells provide the needed oxygen carrying capacity while sparing the already compromised cardiovascular system. Even moderately severe cases of acute gastrointestinal bleeding can be effectively managed with packed cell transfusion alone or combined with modest amounts of whole blood. The central venous pressure is an excellent guide in such patients. With high or even normal values circulatory overloading followed by heart failure is a distinct hazard best avoided by transfusing cells rather than whole blood. At times it may even be necessary to resort to a modified form of plasmaphoresis in which anemic whole blood is replaced by packed cell transfusions.

Surgical patients, both before and after operation, are candidates for transfusion of packed cells rather than whole blood. There is no evidence that plasma factors are helpful for most of these persons. In those few instances where a protein deficiency needs to be corrected the small amount of protein in the plasma from a unit of whole blood is insignificant. Such patients require specific treatment with albumin or other protein fractions.

It has been traditional to use whole blood to replace blood loss at surgery. There is no doubt that this will continue to be the general practice, but more and more physicians have found that packed cells can be used just as effectively for the first or second transfusion during surgery.

Packed or sedimented cells are the component of choice for *all* patients who do not have a specific, definite, and good indication for whole blood. This is because:

1. Packed cells minimize the possibility of circulatory overloading and cardiovascular failure.
2. Packed cells minimize transfusion reactions from plasma factors.
3. The incidence of hepatitis may be lower with packed cells than with whole blood.
4. Packed cell transfusions can be given in less time than whole blood.
5. Minor side transfusion reactions from donor antibodies are eliminated when using packed cells.
6. Interdonor incompatibility is eliminated when using packed cells.
7. With packed cells group O donors can be used with relative safety for recipients of all groups.
8. The use of packed cells allows each blood donation to serve more than one patient. Such component therapy is essential for the most effective use of the nation's blood resources.

The time has come to reverse our clinical thought patterns about blood transfusion. Packed cells should be given routinely when transfusions are needed—whole blood should be reserved for special indications.

J.R.B.

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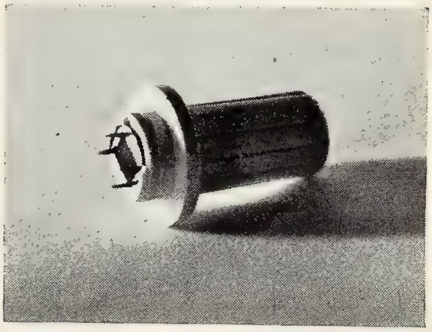

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Symposium

on

The Clinical Aspects of The Psychological Development of the Child

Melvin Lewis, M.D., Guest Editor

Childhood and adolescence are complex phases in human development beyond any one field of study. As clinicians confronted with children with (or without) problems, we draw on many different but related scientific disciplines to help us understand that development. This symposium attempts to bring together some viewpoints that are especially relevant to the psychological development of the child.

Certain general principles are common to all the viewpoints expressed in this symposium. The concept of an invariant stage sequence of development, influenced by maturation and environment, leads to the concept of phase-specificity for the development of object relations, the mastery of developmental tasks, and learning. The tendency toward relative autonomy and endurance of function (psychic structure formation) operates throughout all the multiple lines of development. The concept of the complemental series is useful in understanding etiology and behavior. At all times the individual performs as a whole, a mass action effect concept which is useful in understanding the child with so-called minimal brain damage.

At the same time divergent theories of psychological development challenge the investigator to sharpen his concepts, devise methodologically sound studies, and contribute further to our understanding of human behavior. In our striving toward a unified theory of behavior the boundaries between disciplines are a constant barrier to progress. However, at the present time there are signs of increasing collaboration between the individual clinical specialties, and between the clinical specialties and the laboratory sciences.

It is to be hoped that the contributions from Pediatrics, Psychoanalysis, Psychiatry, Psychology, and Education in this symposium will be the forerunner of a still broader base for the study and understanding of development during childhood.

DR. MELVIN LEWIS, Associate Professor of Pediatrics and Psychiatry, Child Study Center, Yale University.

Some Major Historical Roots of the Child Development Movement in the U.S.A.

Milton J. E. Senn, M.D.

The presentation of an adequate and valid history of the child development movement in our country demands a detailed and adequately documented record. This is beyond the scope of the writer at this time. What is more realistic is an account of some of the more obvious influences. It is hoped that the reader will feel some degree of curiosity and interest from reading about a movement which has become a major development in American medical and social science.

Pre-American Influences

Concern about children extends backward in time to earliest recorded history. This was expressed usually as random thoughts about their education, physical health, character and reputation which appeared in essays on a variety of subjects. Acknowledgement that the early years of life are important precursors of what the later years will bring forth is not an invention of Freud or modern psychologists. It is a theme which extends forward from earliest time in the writings of essayists, poets, dramatists, philosophers, and physicians.

Plato in The Republic said, "The direction in which education starts a man will determine his future life." Again, he reminds us that "in childhood and youth their study, and what philosophy they learn, should be suited to their tender years; during this period while they are growing towards manhood, the chief and special care should be given to their bodies that they may have them to use in the service of philosophy."

Plutarch in his Essays on Love, The Family and The Good Life expressed tenderness for little children, recommended breast feeding for molding an infant's body, and lessons which would "regulate the character of children from the beginning."

Even in the days of the Greeks and Romans there was concern about discipline, and polar differences in opinion existed between those who favored severe physical punishment and those who recommended unequivocally the use of exhortation and those rational methods which taught children respect rather than fear. Records of Renaissance families of Italy emphasize the place of the family in the life of the child, and the roles of parents as models for conveying moral ideals and imperatives as the foundations of character.

In the 15th and 16th centuries children were not only clothed as were adults, but their biological and psychological significance was not realized. They were considered miniature adults and even permitted the sexual license of the time, sharing a measure of bawdiness with adults. The concept of the innocence of the child, and the suppression of sensuality came as an influence from the more austere movements in religion of the time, especially those associated with the Jesuits' system of education.

Comenius, the last Bishop of the Old Church of the Moravian and Bohemian Brethren in the 17th century, wrote about the education of the preschool child. His influence with its psychological insight was considerable in Europe even into the 19th century, and his principles of education are recognizable in our modern educational system. (Comenius, by the way, is to be further distinguished by having turned down the presidency of Harvard College in 1624.) Other theologians, in Britain especially, resorted to biblical references in prescribing measures for the proper rearing of the child and his education. Their focus was on his character, his soul and much more than on his physical and emotional wellbeing. The high infant and child mortality of the time convinced them of the inevitability of early death and the need to plan for salvation and life after death. In the same century, John Locke, the physician-philosopher although a life-long bachelor, wrote advice on children for his friends. Like the earlier Greek philosophers he talked about postnatal care as well as about the nature of man and the moral training and education of children. Locke anticipated some of the present-day theories of the use of discipline in promoting character development, weighing the

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DR. MILTON J. E. SENN, Sterling Professor of Pediatrics and Psychiatry, Child Study Center, Yale University.

benefits of rewards and punishments in moral training. Locke disbelieved that the child had a tendency to sin, but he continued as others before him to see the child as a miniature adult who needed guidance from rational teachers to bring him out of childhood into adulthood.

But it was left to Jean Jacques Rousseau to emancipate the child from the most constrictive considerations. In a number of his writings, particularly in the famous Emile, Rousseau maintained that childhood is "natural," that it is a time important in itself; when the behavior of the child is appropriate to the demands of his needs and to those of his world at that time. Rousseau suggested that the child be given less supervision and direction by adults and be permitted to grow from his own natural potential. In a way it was natural that Rousseau whose life glowed with his own paternal shortcomings and his varigated sexual experiences should not stress the theological or evangelical, but rather the rational and secular. It is interesting that Rousseau like so many others concerned with the nature of child and his character, would include advice on breast feeding. For example, he suggested that a baby's own mother should feed an infant her milk rather than a wet nurse, because "does not the child need a mother's care as much as her milk?" He is one of the few child guidance writers who also considered the role of the father. "The real nurse is a mother, and the teacher the father; let them agree in the ordering of their duties as well as in their method, and let the child pass from one to the other." The writings of the 18th century Rousseau are recommended to all persons concerned with present-day education, child rearing and ego psychology. This restless Swiss who seems so different from the average citizen of that country these days, had a counterpart of sorts in a second remarkable Swiss named Pestolozzi. Moved by Rousseau's political and social agitation, he wrote a series of articles and books on pedagogical methods which had a train of influence through Froebel, Montessori and John Dewey, each of whom in turn had a profound influence which is still felt in present-day educational practices. Pestolozzi believed in the innate goodness of children, their potential for learning, and he anticipated the American Head Start pre-kindergarten program of recent years in emphasizing the moral duty and responsibility of citizens for educating the poor as well as the rich.

It is not widely enough known that Darwin's work on evolution influenced the history of child psychology, and that his speculations had a direct effect on the study of man since he assigned scientific value to descriptions of childhood behavior. He was one of many scientists making what have been called naturalistic observations who began their studies on their own children. Such research today is exemplified in the important contributions to cognition of still another Swiss, the philosopher and epistomologist Piaget.

Darwin taught that by careful observation of the infant and child one could see the descent (or ascent) of man. He not only pioneered in the scientific study of the child, but his ideas and research found expression in the studies of modern social scientists in the manner in which they conceptualize the development of societies. The enmity of theologians which Darwin encountered is well known, and much of it came about because of his ascribing signs of man to animal life. Yet social scientists credit him with the discovery of comparative psychology and with setting a model for present-day research in animal behavior. For example, the school of ethology headed by Lorenz and Tinbergen, finding relevance in studies of behavior of lower animals and birds to research of humans is following the example set by Darwin. American research today on infant behavior includes observations of primates as well as humans.

American Influences

The early American Colonists brought to this country attitudes and opinions about child care and rearing which carried the benchmarks of British and European philosophers and theologians. The doctrine of "natural depravity" prevailed generally in the community and so it was that persons came to regard their children as being "filled with the devil." Jonathan Edwards, of Yale College fame, called children "vipers." But Anna Bradstreet, one of our earliest Puritan poets and a mother, saw children differently. "Diverse children have their different natures: some are like flesh which nothing but salt will keep from puterfaction; some again like tender fruits that are best preserved with sugar. Those parents are wise that can fit their nurture according to their nature."

The pedagogues who took the lead along with theologians in advising parents on the education and rearing of children, assumed with them that children were born into sin, and like their parents needed the protection and saving grace of religion. Secular education was as much concerned about religious matters as that stemming from formal religious training. Except for descriptions of children's behavior, dress, habits, and problems which appeared in the general literature and in treatises dealing with education secular and religious, there were (little) reports of what might be called scientifically made observations, and no research as such.

However, the last years of the 19th century mark a beginning, although a small beginning, in studies of child behavior. These were isolated "naturalistic" reports like the early work of the naturalists who observed outstanding events in the march of the seasons. These investigators approached their subjects directly, and more or less naively, with little concern about methods or other perplexities of their work. An outstanding educator of that period was G. Stanley Hall who later became President of Clark University. Hall was influenced by the German, Wilhem Preyer, who studied infants and recorded their behavior item by item, week after week, antidating the work of Arnold Gesell and his developmental examinations. Preyer's work was physiological and philosophical but it influenced greatly the history of child psychology. Hall, a remarkable man in many respects, was the founder of American psychology, the teacher of many other innovators particularly John Dewey, Gesell and Terman, the originator of the first psychological laboratory in America, and the person who brought Freud to the U.S.A. for his only visit to our country. By his particular interest in adolescence, Hall espoused the cause of child study as well as of psychoanalysis. Needless to say, a person who defended psychoanalysis then, as even now, was criticised for being unscientific. It is true that the questionnaire method, which Hall introduced for child study, has since been proven to be less scientific and reliable than many wish it to be. Yet it served a useful purpose as it focussed attention on child study as a legitimate field of study and demonstrated the evolving characteristics of children in their development.

The beginning of the 20th century showed child study to be well established as an independent discipline. The first part of the century cannot be characterized as brilliant in this regard. Research consisted of biographical studies, questionnaires filled out by teachers and parents, and products of research had a limited circulation despite the publication by Clark University, of Hall's "Pedagogical Seminary." More systematic attempts to study child behavior and child development began in the 2nd decade of the 20th century. They were focussed primarily upon the assessment of specific traits and capacities, tended, to deal with problems of psychology involving the relation between two variables, but began to utilize methods of investigation which are in common usage today. The predominant search for methods focussed around purely quantitative and objective measuring tests, as was the manner of this scientific age.

The work of Binet and Simon was a major influence of American psychologists, and from then until the present day the child development movement has included many persons who are particularly interested in measuring and comparing.

Ellen Key, a Scandinavian woman philosopher, named the 20th century "the century of the child" and her prophecy was realized in the period beginning in the second decade of that century. There was from then on a great interest in children, and a belief that by starting to influence a person early one could improve people greatly, whether they be single individuals or even nations, and hence avoid some of the personality difficulties of adults and of large societies which have seemed so alarmingly abundant and severe in this century. It became highly desirable to "study" children and to develop new patterns of child care and rearing in families and in elementary and even pre-schools. Among the important developments of the 1920's was the progressive education movement. Associated with this was the formation of the nursery school. John Lewey in progressive education, and Lucy Sprague Mitchell and Abigail Eliot in the nursery schools which they founded, considered their programs educational in the sense of helping children learn. But they were as interested in the very processes of learning as well as in techniques and curricula, and each new project became an experiment into itself.

Another major development of the 1920's was the establishment of the child guidance clinic for treating disturbed and delinquent children and youth. The first of these in St. Louis, lasted but one year because it was said to have had little influence in lowering the crime rate. The child guidance movement faltered but did not die. Under the direction of Dr. William Healy at the Institute for Juvenile Research in Chicago, the child guidance clinic there became firmly established and became a model for similar psychiatric clinics for children over the country. Dr. Arnold Gesell in 1926 established at Yale a "guidance" nursery for young children who came for observation and testing. This differed in having no psychiatrists or social workers on its staff.

One hears much these days about social and community psychiatry as if it were a modern invention. Actually it started in the 1920's when psychiatrists emerged from state hospitals and private institutions to provide treatment for adults and children on an outpatient basis; they became involved in schools as well as with community social agencies, and often traveled over the rural areas in so-called Mobile Child Guidance Clinics. Connecticut pioneered in this endeavor.

American psychiatry, concerned with individual patients or with problems of communities was profoundly influenced by Adolf Meyer at Johns Hopkins, but who also stimulated child psychiatrists to view human development as proceeding naturally along certain lines, and in evolving out of the relationships between individuals and other forces in the environment. Meyer taught psychiatrists as well as pediatricians how to make a "life chart" of each patient studied. This graphically helped a physician see relationships between events and circumstances in the life of an individual. Meyer's teaching paralleled in time the influence of Freudian psychology which became strongly manifest in the late 1920's, first in the treatment of individual children and then in the techniques of child rearing, child care, and education.

As mentioned before, the early 1920's found child development research concerning itself with psychometrics, especially in regard to assessment of the feeble-minded. This led to bitter controversy over the issue of "nature versus nurture." Some psychologists and sociologists maintained that intelligence was largely the product of child rearing and life experiences, while geneticists asserted that intelligence was inherited. The controversy illustrates the attempts to establish a simple cause and effect relationship for behavior. It was not until quite recently that this approach was more or less abandoned in favor of a multidimensional concept of human development and behavior.

The 1920's found a few prominent psychologists, educators and psychiatrists decrying the paucity of information about children and their development and fostering the establishment of Centers where children could be studied, and scientists trained through Fellowships to make more scientific approaches to the study of children. In 1924-1925 the National Research Council changed the name of its "Committee on Child Psychology," to "Committee on Child Development" in order to stimulate Fellowship training and get candidates for degrees in social science to enter some of the new centers which were being started in a few universities to specialize on child research. The American Psychological Association did not recognize child psychology until some years later, after various child research centers had been in operation. The development of these centers constitutes a major influence in the American child development movement. Yale, the state university of Iowa, Teachers College of Columbia University and the Merrill-Palmer School in Detroit were pioneer centers. They were helped financially through generous gifts of the Laura Spelman Rockefeller Foundation. If any one person were to be singled out for the most credit for sponsoring the child development movement in our country from the mid 1920's until the present time, it is Mr. Lawrence K. Frank. It was his influence as a staff member of the Laura Spelman Rockefeller Foundation, and later of the Josiah Macy Jr. Foundation that encouraged philanthropic giving in the creation and sustained support of these research institutes.

These institutions were not only outstanding because of their research on systematic observation of individual children, but are also to be credited with the development of experimental nursery schools for the study of children as individuals and in groups, and for the establishing of programs of parent education. Not only were individual parents of nursery school children taught, but many of the centers in the pioneer group, as many others which followed, set up extension classes for groups of parents in conjunction with public school systems, churches and social agencies.

The role of a few physicians and medical educatos has been prominent along with other professional workers in fostering the child development movement and its various working units. Dr. Arnold Gesell has already been mentioned for his contributions to the understanding of human behavior through his observations of infants and older children. Gesell at Yale was also responsible for that institution becoming the first to accord developmental status in a medical school to the new field of child development. On Gesell's retirement from Yale in 1948, the Child Study Center was established with even broader commitments in the university, having not only a place in the medical school, but active cooperative roles in the Graduate School (especially the Departments of Psychology and Education) and to a lesser extent in the Law School. The staff of the Child Study Center works most intimately with colleagues in pediatrics and psychiatry.

Interest in behavior was not the exclusive concern of the child development workers in the 1920's.

Anatomists at the University of Minnesota and at Western Reserve Medical School studied physical development of infants and children, being pioneers in making comparative studies of skeletal development and then of other items in healthy babies and those sick and malnourished. Their research stimulated and influenced pediatricians to appraise physical growth.

From the early 1930's onward, the history of child development in the United States glows with the names of many persons who have made important contributions to our understanding of the growth, development and health of children, and to improvement in their rearing and care. The list of contributors is too large for inclusion here. However, one must mention Alfred Washburn of Colorado who pioneered in longitudinal studies of the same human subjects beginning in infancy and continuing through young adult life, emphasizing not only the physiological aspects of development but the psychological as well. Harold Stuart, a Boston pediatrician is another. He compiled and edited a volume of research findings on child development for the 1930 White House Conference. With Dr. Kenneth Blackfan, Professor of Pediatrics at Harvard Medical School, he had established a system of making periodic measurements and tests including X-ray assessments of babies and children until they became young adults. A group of investigators under Dr. Lester Sontag at the Fels Fund Center for Child Research at Yellow Springs, Ohio has made many contributions of techniques and instruments for medical and physiological appraisal of developing children.

In 1934 the Society for Research and Child Development was organized as a multi-disciplinary association to provide meetings of those engaged in child research and to issue publication in that field. This testified to the burgeoning interest in the field and to the great accumulation of important scientific data. Unfortunately, much of the data was never used; in fact, even with the development of special publications, many projects remained buried and unavailable for use in the care and education of children. Too frequently one hears the statement made even today, "we don't know much about children's behavior and so we don't know what to do for them." This remark shows ignorance of or disinterest in bibliographical research. Whoever is interested to seek will find many excellent studies which have been made and which have practical importance. It is interesting to see in the literature today remarks about the importance of infant behavior and the need to study humans in the early years because one may find there clues to later personality development. Present-day discoverers of the importance of early infant behavior seem not to be aware of the work of the investigators in the 1930's who already then demonstrated clearly the uniqueness of each individual and the relevance of early experiences to later life behavior.

The term child development is now widely accepted as a concept for research, but we still lack a conceptual formulation that embraces the development of the child from fertilization to senility, nor do we fully comprehend the multi-dimensionality of his organism. We still use methods of study which are irrelevant and inadequate for a multi-dimensional approach. Too frequently children are studied by persons of different disciplines who do not focus on the same children, and make comparisons with lower animals or with other subjects which are inappropriate. In the words of Lawrence K. Frank, "while the cumulative product of research over the years is indeed impressive, it is not unfair to say that the problem of human growth and development awaits formulation as a process, exhibited by an organized whole, which can and does produce different products depending upon when, where, how and in what quantities and intensities that process operates."

Today we have a number of promising leads for the development of useful models for child development research. We also have more money than ever before because of the interest of our government, particularly through its various Institutes of Health. The Congress has shown its interest in children by allocating large and increasing amounts of money for the care and study of children. One far-reaching result has been the establishment of a new National Institute of Child Health and Human Development in Bethesda, and several departments or institutes of child health and development in universities, more recently attached to the various departments of pediatrics. Beginning with an interest in the mentally retarded, then with the psychologically deviant, there now is tremendous interest in such institutes in the normal and healthy child. They bring together investigators from many disciplines both within and outside medicine, for conjoint study of the growing infant and child. It is with some pride that I report that since 1948

Yale University has long pioneered in such endeavors. The staff of the Child Study Center has demonstrated the practicality and usefulness in research, teaching and public service of joining with colleagues in the departments of pediatrics, psychiatry and psychology in mutual enterprises aimed at helping parents and children of every class, of every economic group, and of every condition of the mind and body. We approach the 21st century with a history of productive research and abundant community service behind us, but with a promise of much greater things to come.

MEETINGS

PSYCHIATRY

June 12 **1:30 P.M.**

Personality Development and Psychopathology

Kettle Building, Norwich Hospital

Sponsored by the Connecticut Postgraduate Seminar

Speaker: Maurice E. Linden, M.D., Director of the Division of Mental Health, Community Health Services, Philadelphia, Pa.

Contact: Vincenzo Cocilovo, M.D., Assistant Superintendent, Norwich Hospital

SURGERY

September 4-December 4

Eleventh Series of Postgraduate Courses for Specialists in Ophthalmology

Postgraduate Institute of The New York Eye and Ear Infirmary, 310 East 14th Street, New York, N.Y. 10003

Contact: Jane Stark, Registrar

GENERAL

June 12 **4:00 P.M.**

Connecticut Society of American Board Internists, Annual Meeting

Les Shaw's, New Haven

Speaker: Alvin Feinstein, M.D., Associate Professor of Medicine, Yale University School of Medicine

June 16-20

117th Annual Meeting, American Medical Association

Brooks Hall, San Francisco, Calif.

June 16-20

American College of Preventive Medicine

San Francisco

June 17-19

Intensive Care Units

University of Colorado Medical Center, Denver, Colo.

Sponsored by the American College of Physicians

Fees: A.C.P. Members $60; nonmembers $100

Contact: Edward C. Rosenow, M.D., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia, Pa. 19104

June 17-19

American Neurological Association

Washington-Hilton Hotel, Washington, D.C.

June 19-21

Infectious Disease: Mechanisms and Manifestations

University of Maryland School of Medicine, Baltimore, Md.

Sponsored by the American College of Physicians

Fees: A.C.P. Members $60; nonmembers $100

Contact: Dr. Rosenow

June 23-28

Educational Conference in Environmental Health

Sheraton-Park Hotel, Washington, D.C.

July 22-24

Air Polution Medical Research Conference (AMA)

Denver-Hilton Hotel, Denver, Colo.

August 1-3

Conference in Dermatology

Aspen, Colo.

August 25-30

American Physiological Society (International Congress)

Washington, D.C.

August 26-29

2nd Western Hemisphere Nutrition Congress (AMA)

Americana Hotel, San Juan, P.R.

August 28-30

Society for the Study of Reproduction

Vanderbilt University, Nashville, Tenn.

Psychosexual Development and Sexual Behavior in Children

Melvin Lewis, M.D.

Introduction

The first systematic account of the psychosexual development of children was attempted by Freud in "Three Essays on the Theory of Sexuality" (Freud, S. 1905). An instinct, or drive, was defined first of all as "the psychical representative of an endosomatic, continuously flowing source of stimulation . . ." Another way of defining an instinct is that it is ". . . an elementary urge, rooted in bodily tensions, which environmental influences may deflect from its course and modify in many ways but probably cannot eradicate" (Waelder 1960). A further point to be considered in the definition of the sexual drive is that its object and its aim must be taken into account as well as its source. Once this is realized, we are able to see that the sexual drive changes in its object and its aims as the individual proceeds in his development. There is, in fact, a sequence of development in sexuality in its broadest sense, just as there is in thinking, motility, speech, and so on, from rudimentary elements to complex, mature, relatively autonomous functioning (Neubauer 1967). Furthermore, the sexual instinct does not follow a simple line of development—its development is intimately involved in all the many other simultaneous lines of development (Freud, A. 1965).

Before describing this development, the sources of evidence should be mentioned. Four major sources of evidence are available for study. Historically, the first source was in the recovery of early infantile feelings that occurred during the psychoanalysis of adults (e.g., Freud 1909a). Second, remnants of infantile sexuality have been observed in normal adult behavior, as well as in psychological disturbances in adults, such as the sexual perversions, eating disturbances, gastrointestinal disturbances, and certain characterological disorders (e.g., Abraham 1924, 1921, 1925). Third, the analysis of children continues to contribute a rich source of evidence (e.g., Freud 1909b, Bornstein 1949). Fourth, direct observation of children has made available additional data (e.g., Spitz 1965). It should be remembered, however, that just as certain behavior may represent infantile sexuality even though it doesn't look "sexual," other phenomena which for all the world may look "sexual" may not necessarily represent infantile sexuality. For example, a penile erection surely looks "sexual," but in infants and children penile erections may occur regularly in association with R.E.M. sleep, and may then represent a metabolic change as well as a psychic event (Fisher 1965).

Psychosexual Development

Let us return now to the development of infantile sexuality, bearing in mind the aim and the object of the sexual drive. Take, for example, the sexual aim of a young infant. The aim is simple: to obtain a feeling of pleasure and satisfaction and relief of discomfort by the most immediate means possible. The young infant derives pleasure from a wide variety of visual, tactile, kinaesthetic and auditory stimuli—but by far the most sensitive and greatest source of pleasure is in the region of the buccal mucosa. We also see immediately who is the object of the sexual instinct in the infant—it is the infant himself, or an extension of himself, in his autoerotic activities such as mouthing and sucking of the breast or the thumb (notice immediately how we cannot isolate sexual development from the development of object relations).

As the infant develops, and speech and the capacity for symbol formation emerges, the child begins to experience feelings about his separateness and his own worth. He develops a sense of autonomy which has to be reconciled with his ambivalent feelings, all at about the same time that he is acquiring a new skill—that of sphincter control. This new region, the anal mucosa, now becomes erotogenized, and serves the aims of his ambivalent feelings towards the adult objects in his world who are now "disciplining" him. The young child may express his ambivalence in the holding on and letting go of his bowel movements. This am-

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DR. MELVIN LEWIS, Associate Professor of Pediatrics and Psychiatry, Child Study Center, Yale University.

bivalence may also be expressed in the controlling and clining behavior seen in some 2 and 3 year old children.(Notice again how other lines of development, notably object relations and cognitive development, subsumed under the general heading of ego development, contribute to the form of sexual development.)

It is when the child is between 3 and 6 years of age that we see behavior that is more clearly recognizable as "sexual" to adults who think in terms of the genitals. The child at this stage is very much aware of the anatomical differences between the sexes, and is curious to a degree about pregnancy, childbirth, and death. Sometimes this interest is represented in the play of the child, who becomes absorbed with toys that involve filling and emptying, opening and shutting, fitting in and throwing away, building up and knocking down. The opportunities for the sequential development of play in childhood thus becomes as important for the sexual development of the child as it is for other purposes (problem solving, mastery of body skills, functional pleasure in play, coping with anxiety, facilitating object relations, communication purposes, etc.). The child at this stage experiences intense sexual and aggressive urges towards both parents, but the aim is less well defined. To be sure, the little boy wants to marry his mother, or the little girl will play with dolls and "have babies," or they both will be absorbed in fairy tale or television characters that represent their own fantasies. Such fantasies also emerge in the dreams of children. Children of this age may also play at mothers and fathers—or doctors and nurses—towards a partial fulfillment of their sexual aims, which at this time may be partially fused with their aggressive fantasies. It is not uncommon, for example, for boys and girls to inflict pain on each other in keeping with their understanding of the sexual act as an act of violence. They may also be quite exhibitionistic and possessive, especially of the parent of the opposite sex.

Between 6 and 12 years of age, during the elementary school years, concepts of inevitability regarding birth, death, and sex differences become clarified, and the sense of time and the ability to differentiate between fantasy and reality become established. Ego defense mechanisms are strengthened, and the child consolidates earlier reactions such as shame against exhibitionistic urges, disgust against messiness, and a sense of guilt that contains sexual and aggressive wishes. The child's play at this time is usually characterized by organization, whether in a board game or team game. Sex play continues, with voyeuristic tendencies and the urge to touch, but usually the sex play is more discreet—that is, adults see it less often. The object of the sexual instinct is a peer, but the actual playmate may be of either sex, as we shall see later.

When puberty comes, the young adolescent struggles to achieve mastery of his body and his sexual and aggressive urges, at the same time as he is trying to separate from his family, find new, appealing sexual objects, and achieve a sense of identity. In the course of this struggle the sexual behavior of the adolescent may range from an indiscriminate regression toward expressions of earlier forms of the sexual drive, manifest in impulsive behavior, messiness and alternating labile affects; to petting and mutual masturbation, which may be heterosexual or homosexual. Sometimes earlier aims and objects are temporarily gratified and used, as observed, for example, in isolated acts of fellatio, or in exhibitionistic behavior. Occasionally one sees an adolescent sexually molesting a young child, especially during baby sitting. Such adolescent boys are usually identified with a dominant mother.

Ultimately a mature primacy of the genital zone is established, with an appropriate heterosexual object choice and appropriate achievement of the new sexual aims of a love relationship, sexual intercourse, orgasm, discharge, and childbirth.

Masturbation

Masturbation, of course, occurs throughout childhood but its form, as well as its accompanying fantasies, varies with the development of the sexual instinct. Although the term masturbation in its ordinary sense is understood to represent self-stimulation of the genitalia, in its technical sense it means the gratification of the sexual drive by the self or an extension of the self. Thus, the mouthing behavior of the infant is in this sense a rudimentary form of masturbation in that it is a manifestation of antoerotic activity in which the primitive sexual drive is being gratified by the self. The pleasures involved later in having a bowel movement also have a masturbatory component for the young child.

Direct manipulation of the genitalia reaches its first peak somewhere betwen 3 and 4 years of age, although accidentally touching of the genitals may occur in very young infants. An interesting observation is that foundling home infants deprived of object relations do not play with their genitals, even in their fourth year, while family raised infants with good object relations play with their genitals toward the end of the first year (Spitz 1962). More disguised masturbation takes place in the course of "horse play," when the child contrives to rub his or her genital area against, say, the knee of an adult.

Masturbation reaches its second peak during adolescence, accompanied usually by fantasies of undressing, exposing, and touching. At this stage group masturbation may occur.

Girls probably derive sexual satisfaction by stimulation in the region of the clitoris rather than the vagina, and this remains true of adult women who achieve orgasm most regularly from stimulation in the region of the clitoris. In fact, it appears that there is no such thing as a vaginal orgasm distinct from a clitoral orgasm (Masters and Johnson 1966; Sherfey 1966).

Masturbation is a normal phenomenon, but like eating habits and bowel training, in the general interests of social relationships its practice is usually subjected to normal social rules. Indeed, it has been suggested that cultures which permit the unrestricted gratification of the sexual urge during the elementary school years and early puberty have a large proportion of the people whose level of personality development and intellectual functioning is lowered (Spitz 1962). Open masturbation in company is of course to be discouraged. Compulsive masturbation in private is best regarded as a sign of tension or disorder whose sources should be relieved before masturbation itself is curtailed. Occasionally a child will become addicted to masturbatory stimulation. Under no circumstances should threats of punishment be made. Children of all ages must be given the opportunity to masturbate

Adult Attitudes Toward Childhood Sexuality

It is necessary now to examine how the attitudes and practices of adults may influence this development of the sexual drive in children. At each stage in the development of the child, the adult provides at least three factors: viz., 1) excitatory, 2) inhibitory, and 3) models for identification. If we return now to the sexual development of the child with these three factors in mind, it will become clear how the adult influences the child's sexual development.

During infancy sexual excitement is aroused by adults in several ways. There is first of all the involuntary and inescapable seduction by the mother when she diapers her child. Sometimes a mother or nurse will unscrupulously masturbate an infant to pacify the child. Most children perceive, by sight or sound, adult sexual intercourse by the time they are $1\frac{1}{2}$ years old. And of course what passes for "horsing around" is often sexually exciting for a child. Sometimes the excitation is beyond the child's tolerance.

> A 4 year old boy was recently brought to the emergency room at 4:00 a.m. in an acutely agitated state. For the previous four hours he had said there were spiders under his pajamas and there were shadows inside of him. While in the waiting room he screamed as his aunt attempted to keep a coat over his completely nude body. He refused to wear any clothes at all, and remained unashamedly stark naked!
>
> On further study it was found the boy and his mother slept together. There was a serious marital difficulty, which included a severe sexual problem and violent behavior between the parents, who slept apart.
>
> Later we learned that the boy's mother would often allow him to sit on her lap. He would feel her pelvis and ask her why she did not have the same feeling his father had. He would also be allowed to fondle his mother's breasts, and his mother noted that he would get an erection at the slightest touch.
>
> It became clear that his fears about wearing his clothes were his way of reassuring himself and allaying his castration anxiety by keeping his genitalia always in sight. His symptoms subsided with treatment and advice to his parents, especially his mother, to stop the sexual over-stimulation.

In fact, every child should have his own room, and this should begin at once—certainly within the first few months.

Covert seduction and sexual arousal may also take place when a parent spanks a child (Lewis and Sarrel 1967).

> Carol, aged 8 years, developed severe unexplained vomiting following a minor virus infection. She appeared markedly anxious and frightened. In the course of a psychiatric consultation it was discovered that Carol's parents had separated and Carol was now living alone with her father. Carol's father seemed to talk of Carol as though she were his wife. Carol's father had also taken frequent rectal temperature readings of his daughter during her "illness."

In further interviews Carol revealed how her father would spank her across the buttocks; he would carefully take off her panties and put her across his knees. Further, Carol and her father would sit in a love seat together, and her father would put his arms around her. He would then turn down the light after the television was over. Carol described this as "adventurous"—but also "scarey." On weekends Carol would be encouraged to sleep in her father's bed. Carol also saw her father as dangerous. He kept a gun in the house, and after drinking he appeared to Carol to be somewhat glassy-eyed, and looked angry.

Carol eventually revealed her anxiety as she produced a vomit and blurted out. "Parents shouldn't be like this, I'm ruining my life!"

The situation was discussed with her father, and his seductive behavior stopped. Carol's vomiting subsided and she returned to school to do well. Carol's father eventually remarried.

Children, indeed, should not be spanked.

Occasionally a sexual assault occurs in the course of so-called medical treatment.

At the age of 2 years, Doris developed periodic fevers which were diagnosed initially as pneumonia and treated with antibiotics. Her parents then brought Doris to a medical center in the east where a pelvic examination was performed. The parents understood from this that Doris had an infection in the vagina, and that chloramphenicol douches were to be given daily for one to two months. The parents decided to make an exciting game of this procedure. The game consisted of Doris' father holding her upside down by the legs while Doris' mother inserted the douche. This "game" was carried out repeatedly. Subsequently Doris would play a game with her dolls in which she would stick something between the legs of her dolls. This game was called "Baby hurts"'

The followup of this child came about many years later. When Doris was aged 13 years, shortly after the onset of her menses, she developed abdominal pain which eventually led to a laparotomy and later a pelvic examination under anesthesia. No organic pathology was ever found. Two years later her parents once again brought Doris east for a gynecological consultation. They had though of the possibility of a hysterectomy being performed, and expressed concern that friends and neighbors would think they had brought Doris east to have an abortion.

The gynecologist requested a psychiatric consultation. A mutually seductive relationship between father and Doris was observed, and Doris' mother appeared to facilitate this relationship by frequently arranging to leave father and daughter alone together because she thought "they wanted to be left alone together." Doris looked older than her years, but acted in a child-like manner. She tried to be appealing, but seemed extraordinarily naive sexually; she said she did not know the meaning of the word masturbation. Doris was in turn tearful, coquettish, and angry. Family life centered on Doris, who managed to control her parents. When Doris attempted to express concern about her possible inability to bear children, her affect was bland.

A diagnosis of a conversion reaction in an hysterical personality was made.

The inhibitory attitudes of adults toward infantile sexuality begin early, usually as soon as parents see the child masturbating. The child is unfortunately threatened with loss of love, or with threats to his penis, which are later internalized by the child who then experiences guilt about masturbation, or fears his own instinctual urges.

The model a parent provides for the child strongly influences the child's own attitude to his or her sexual identity. A mother who does not value her own femininity will not be able to help her daughter accept feminine attitudes and feelings. The values of a child are essentially those that been incorporated from those adults the child loves and respects, and such values are inculcated not by lessons but by the countless ways parents and adults reveal to the child their own biases.

Sexual Identity

The gender, or sexual identity, of a child is of course powerfully determined by the attitudes of the parents, even when the anatomical, gonadal, hormonal or chromosomal sex is confused or ambiguous, as in certain cases of intersex and hermophroditism (Hampson and Hampson 1961).

Most children behave like most scientists; when confronted with a phenomenon, they construct a theory to account for the phenomenon, and begin fitting in evidence that supports their theory. Then when they are confronted with a new and unexpected phenomenon, they either try to fit it into their old theory or ignore the awkward fact that doesn't quite fit. It is only with great reluctance that they modify their theory.

So it is when a child discovers his body. He identifies his eyes, nose, ears, and toes and is quite satisfied that everyone has these features. The child then discovers that some individuals have a penis, and some don't. He becomes intensely curious and wants to look at girls who sit down to urinate, and boys who stand up; at daddy who has a big penis, and mommy whom he believes has a penis but it cannot be seen. Perhaps it is inside her body, perhaps it has been cut off, perhaps his penis may some day be cut off. He sees his mother getting bigger, and learns that she is pregnant. He tries to fit this phenomenon into his previous theories.

What are these early childhood theories of the body? Most pre-school children conceive of the body as a kind of sac, filled with a fluid. Vaguely shaped body organs, such as a heart, usually in the shape of a valentine, vaguely exist in this sac. The child arrives at this theory because he observes that when he falls and hurts himself, he oozes fluid. Often the child is frightened at this—the fluid might all leak out. Nothing reassures a child as much as a band-aid placed over a graze; the puncture is sealed, and the wound is hidden from view. But how does a pregnancy arise? The only intake the child knows well is that of food. Therefore to the child it appears that foods must give rise to a pregnancy. And didn't he hear someone say that the baby grows in his mother's stomach? Then how does the baby come out? The only major output the child knows is the anus. Therefore the baby must come out through the rectum just like having a BM.

The child frequently expresses his sexual preoccupations through his attitude toward food. Whereas for the young infant food was virtually equated with mother, for the young child food now becomes linked with his sexual theories, resulting in a number of irrational attitudes toward food. For example, many children have a fear of getting fat determined in part by their fear of pregnancy. Sometimes a fear of being poisoned is a particular result of oral impregnation fantasies. Certain children develop extreme food fads, such as an aversion to the yolk of an egg that contains the chick embryo, or say, sausages; in these cases the food fad represents a displacement and reaction formation against their unconscious cannibalistic and sadistic fantasies. Usually this sexualization of eating eventually gives way to a rational attitude toward food.

One outstanding principle in the education of the child is that one encourages learning and discovery by providing the correct information the child wants at the time he wants it. The 4 year old child is not interested in information about dating —but he is absorbed in questions about his body and how babies are made, and will he die?

It does not make sense to give a child anything but the correct explanations he needs at the time. And if there is something the adult does not understand himself, he should not confuse the child with his own rationalizations and distortions; nor should he duck the questions. Yet many parents do confuse their children further, or put a stop to their child's natural curiosity. Usually this is due to ignorance or sexual difficulties within the parents themselves.

Homosexual and Heterosexual Preference

The normal infant attaches himself to both mother and father by virtue of their parental functions, such as caring and protecting, and is therefore indiscriminately homosexual and heterosexual in terms of his choice of adult object. Between 3 and 6 years of age the young child clearly recognizes the difference in sex in his parents and once more is both homosexual and heterosexual, this time in terms of his attachment to his parents as sexual objects. Later he may once more attach himself to adults more on the basis of function rather than of sex (e.g., his adoration of an understanding teacher, male or female), but in his relationship with peers he may show sexual preferences which are paradoxical. For example, some school-age boys may show a disdain for girls, and wish only to play with other boys. Such boys are not destined to become homosexuals at all; as a matter of fact, the boy who prefers to play with girls at this age is more vulnerable in terms of future homosexuality. The key to understanding this paradox lies in the realization that the choice of playmates at this age is often made largely on the basis of identification, and not of actual love for the selected playmate.

During adolescence homosexual acts occur alongside heterosexual acts. However, the isolated homosexual act of most adolescents is a normal phenomenon and usually represents the adolescent's attempts to merge with an idealized adult, or the adolescent's indiscriminate regression to earlier kinds of relationships where function rather than sex was a predominant factor. However, when an adolescent becomes engaged in a sustained homosexual relationship with an adult, then there is a serious risk of a homosexual identity becoming crystalized. One reason for this in the adolescent male, for example, is that he may find himself unable to give up the invitation to regress to the stage of fantasied fulfillment with the original homosexual object, the father.

Even here it is hazardous to predict what will be the final sexual attitude. A number of factors have to be balanced, many of them unpredictable —seductions, rape, illness, divorce, the child's particular anxieties, the personalities of his mother and father, the opportunities for satisfactions or frustrations, and so on. All we can say is that certain factors weigh in favor of homosexuality, while others weigh in favor of heterosexuality (Freud, A. 1965).

For example, besides the child's genetic endowment, the tendency to identify on a narcissistic basis, the attachment on the basis of early neeeds, the erotizing of the anus through such manipulations as enemas and temperature taking, and the incomplete resolutions of the oedipal conflict may all weigh in favor of homosexuality. On the other hand, the strength of the child's initial heterosexual strivings, his defense reactions against homosexuality, and successful identifications with satisfactory parent models weigh in favor of appropriate sexual attitudes.

Sexual Promiscuity

Parents, especially mothers, are often concerned about the possible future promiscuity of their children, usually the daughter. We don't know all the factors that lead to promiscuity and the frightening rate of out-of-wedlock pregnancies among adolescents. But we know some. Often a young adolescent girl may be acting out the unconscious wish of her mother to have an affair, or produce/receive the gift of a baby. Occasionally the adolescent girl may be repeating compulsively the traumatic incestuous seduction that occurred earlier in her life.

> When Cathy was a young girl she lived in a home in which her father was given to violence. When she was about 6 or 7 years of age her father committed incest with her. In later years when Cathy became an adolescent, she found herself involved with a boy who was many years older than herself. He too was given to violence and had a criminal record involving robbery with illegal possession of a gun. At the age of 15, Cathy eventually became pregnant with her 24 year old boy friend.

When a parent has a need to seduce the child sexually, it often happens that the seduction provides a channel for displaced aggression intended for the other parent. The seduction is then a disguised invasion of the child's body, with serious consequences for the child's developing self-image.

Often the sexual promiscuity is a small part of a large problem of poor impulse control that is the result of a host of factors during the upbringing of the child, not least of which are the models the parents set and their own ambivalence toward the child, causing them to act out against the child on the one hand or fail to impose controls on the other hand.

Sexual Deviancy

Boys who dress up as girls are not generally favored in our society. They may do so to win their mother's love, especially when they think their mother actively dislikes boys. In other cases a boy may dress up as a girl as part of his identification with a female person whom he loved but from whom he is separated.

From the point of view of environmental influences the mother of a transvestite boy is indeed often a women who, for a variety of reasons, and in a variety of ways, dislikes men. She will then start a boy off on cross-dressing as soon as he shows enough signs of developing a masculine identity. In other cases the mother does not tolerate any separation of her son; she sees him as an extension of herself and so gratifies him that his identification with her becomes profound and he chooses himself to dress as a girl. The fathers of such children fail to protect the child from these influences, and does not himself present an adequate model of masculinity for the boy (Stoller 1967). Perhaps the most important clinical point in trying to assess whether a child will become a transvestite is the extent to which the child actually becomes sexually excited during the act of dressing up in the clothes of the other sex.

Young girls who dress up as boys are more often tolerated by our society. Indeed, they are often encouraged to do so. Usually such behavior in the young girl serves to counteract her rivalry and envy of boys and to escape from her feeling of guilt for any supposed harm she may think she has done to herself while masturbating.

Sex Attitudes

While it is true that the school, the community agency, the church, television, newspapers and magazines will all influence the child, none will influence the child as much as the parents, and all will influence the child according to the attitude the parents themselves have to such stimuli. Thus it is the attitude of mothers and fathers and teachers and doctors over the developing years that is as important as, indeed more important than, the so-called facts of life. What we convey to a child every day as an integral part of our relationship to the child is what influences the child most. It is in this continuing education toward healthy attitudes about sex that the physician can be of most help to the developing child.

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Learn to accept in silence the minor aggravations, cultivate the gift of taciturnity, and consume your own smoke with an extra draft of hard work, so that those about you may not be annoyed with the dust and soot of your complaints.

—William Osler

Piaget's Theory of Intellectual Development: The Changing World of the Child

Susan Harter, Ph.D.

Among those efforts to probe the mind of the child, the work of Jean Piaget is unparalleled in its scope and its systematic elucidation of those processes underlying the intellectual development of the child. Swiss-born, Piaget has for more than 40 years now brought his knowledge of biology, philosophy, logic, and psychology to bear on the general problem of how the child comes to know his world. Piaget's detailed observations and penetrating insights into the way thought develops have provided us with one of the richest repositories of theory and data about intellectual development ever available. While any comprehensive review of these efforts is beyond the scope of this article, an attempt will be made to select from the wealth of his ideas and observations those which best characterize the essence and importance of his work for students of child development.

Throughout Piaget's writings (e.g., Piaget, 1928; 1929; 1950; 1952; 1954) there is a preoccupation with the basic epistemological question of how one acquires knowledge about the world. Unlike the armchair philosophers of the past, most notably the British theorists of the 17th and 18th centuries for whom this question was also central, Piaget sought a more direct approach to the problem, replacing philosophical speculation with empirical observation. Thus, to answer the question of how knowledge develops and changes, Piaget sought the most natural arena for its occurrence, namely the mind of the developing child. In the broadest sense then, Piaget is to be regarded as a genetic epistemologist, whose primary interest is in illuminating the historical and developmental changes in the relationship between the knower and what is known to him.

For Piaget, the process by which knowledge is acquired is a very active one indeed, beginning early in infancy. His theory of intellectual or cognitive development begins with the central postulate that motor activity is the primary source from which thoughts, i.e., mental operations, eventually emerge. Developmentally, cognitive activity comes more and more to replace motor activity, and perhaps one of Piaget's greatest contributions is to have charted the course of this developmental sequence. The very active and adaptive nature of these processes cannot be understimated in Piaget's system; for as the title of one of his books, *The Construction of Reality in the Child,* implies, it is only out of the child's active encounters with his environment that his knowledge about the world is created. As Tuddenham (1966) has noted: "Piaget contrasts his emphasis upon the active interplay of organism and environment both with the environmentalist view in which experience or conditioning is impressed upon a passive organism, and with the nativist view that intellectual capabilities exist preformed and merely unfold in the course of development [p. 212]."

In Piaget's elaboration of his theory (e.g., 1952; 1954) one sees the very profound influence of his background in biology. In fact not only are many of his concepts foreign to the more traditional approaches to the study of the child, but typically they defy translation into the language of both the psychologist and layman alike. For example, central to his theory are the interrelated cognitive processes of *assimilation* and *accomodation.* The first of these is analogous to the ingestion or assimilation of food, or the "taking in" of light or sound by the appropriate sense receptors; in terms of intellectual development, assimilation refers to the organism's "taking into" the cognitive system certain aspects of the environment. Thus, such aspects or objects become incorporated or assimilated into the system, and become organized into patterns of behavior or *schemas* in Piaget's terminology, as a result of the organism's action on the environment. For example, when the infant first puts his thumb to his mouth he may suck it in much the same manner that he previously sucked the nipple of his bottle; in so doing, he assimilates the thumb to his existent stimulus-response pattern or schema of sucking. That is, he has extended his sucking

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schema to now include a new and slightly different object or aspect. Thus at this level of development, assimilation refers to the incorporation of both the sensory and motor components of a behavioral act into the existent schema they have activated. At more complex levels of later development, assimilation refers to the tendency for the child's cognitive apparatus to incorporate ideas and new information into the organized system of thought schemas.

Accomodation, conversely, is the process whereby the organism must adjust to, adapt to, or accomodate its functioning to the specific features of the object it is trying to assimilate. Thus, in the example noted above, when the infant attempts to suck his thumb, he must *modify* his previous pattern of sucking behavior in order to accomodate to the somewhat different contours of his thumb. Stated somewhat differently, the pressure of the environmental circumstances leads to a simple modification of the action affecting them. Thus it is the process of accomodation, occurring when the organism attempts to assimilate a new object, which results in behavioral change in the organism, the elaboration of schemas, or in more conventional terms, new learning. At higher levels of development, accomodation refers more to the establishment and coordination of concepts to each other and to external reality. For example, the very young child may initially call all animals "doggie" until he learns to recognize that different species have different names, and that all may be classified under the broad category of animals.

Although assimilation and accomodation are distinguishable at a conceptual level, this is less so in the behaving organism where they both adaptively occur together. That is, every assimilation of an object to the organism involves an accomodation of the organism to the object. It is this reciprocity or equilibrium between processes which characterizes intellectual functioning for Piaget, and provides the model for cognitive development. For once an idea or an object is assimilated, it tends to change the cognitive structure to some degree, which in turn makes possible further accomodatory extensions.

One additional consideration in Piaget's formulation deserves special mention since it represents the necessary link making possible cognitive progress throughout the entire range of intellectual development. One may well ask of Piaget just what impels these processes to function in the manner he suggests. This question may be rephrased in more conventional terminology to read: what *motivates* the organism or the cognitive system to function in such a manner. Piaget's answer, while it may not appear wholly satisfying, is a very simple one: schemas are necessarily, by their very nature, activated whenever they are confronted with objects or information which can be assimilated and to which the organism can simultaneously accomodate. Here Piaget takes his biological metaphor quite seriously in his allusion to hungry schemas which continually demand nutriment. More importantly, such cognitive nutriment can only be provided by those relatively novel objects and events in the environment which lie just beyond the particular level to which the schemas have been developed and organized. Thus, Piaget does not concern himself with explanation beyond the simple postulation of an intrinsically-based characteristic for these processes to function in and of themselves. In so doing, he evades the typical "why should this be so" questions which have plagued students of behavior and motivation on the American scene for so long.

Instead, Piaget's primary concern is to demonstrate that concepts, schemas, or intellectual operations acquired through the interaction of the organism and the environment are attained sequentially in a highly lawful and systematic progression. In this regard, Piaget shares the concerns of other great developmental thinkers such as Freud, Werner, and Gesell, each of whom was impressed with and sought to illuminate the nature of the universal, and therefore exceedingly predictable change in certain behaviors which they observed to occur in the maturing child. For Piaget whose focus has been almost exclusively on the intellectual development of the child these lawful changes represent very discrete and discernable *stages* of development each one of which could be characterized as reflecting patterns of cognitive functioning *qualitatively* different from the previous stage. While these stages of cognitive development can be roughly identified with certain chronological age periods, Piaget's primary intent has been to demonstrate the invariant order of this ontogenetic sequence of stages, and to document in detail the qualitatively different processes which characterize each stage.

Piaget has identified four such major stages, each of which will be briefly mentioned here and described in somewhat more detail subsequently. The first is the *sensory-motor stage* (from birth to approximately two years) during which the infant moves from a primarily reflexive organism responding in an undifferentiated way to his environment to "a relatively coherent organization of sensory-motor actions vis-a-vis his immediate environment" (Flavell, 1963, p. 86). The second stage is that of *preoperational thought* (from approximately two to seven years) during which the child makes an attempt to come to grips with the world of symbols and representational thought; however, his conceptual framework is grounded in the reality of his own subjective and egocentric perceptions, and his judgments are neither reflective nor logical. The third major stage is that of *concrete operations* (from approximately seven to twelve years) by which time the child's reasoning processes or mental operations have become logical, and he has an orderly conceptual framework which he systematically brings to bear on the world of objects around him. The fourth and final stage of *formal operations* (from approximately twelve to fifteen years) is characterized by the occurrence of the child's ability to take the final steps toward conceptualization and abstraction. That is, he can bring logical thought processes to bear not only on the real world of concrete objects and facts, but also on the world of the hypothetical.

In identifying each of these stages, the qualitative differences which Piaget describes have to do with differences in the organization and *structure* of the child's thought processes. For the purpose of understanding the nature of Piaget's contribution, such structural features are best viewed as relatively independent of the specific *content* of the child's behavior. This distinction may be illustrated in terms of the child's language development. There are certain universal structural rules which apply to most language learning, although the specific content or the vocabulary of a particular language varies, depending upon the culture. Another illustration of this distinction can be seen within the realm of logical operations. For example, the concept of transitively, i.e., if A is greater than B and B is greater than C, then A is greater than C, can be studied independent of what the particular A's, B's and C's represent. Thus, Piaget directs himself toward the elucidation of the organization of the cognitive structures, processes, or operations characteristic of each stage, with a focus on the dramatic and systematic shifts which occur in this organization across stages.

The reality of such shifts can be more meaningfully illustrated within a behavioral context, namely one of the classic experiments performed by Piaget: two glasses, identical in size and shape and containing the same amount of liquid, are placed before the child. Then the experimenter introduces a third taller and narrower glass into which he pours the liquid from one of the original glasses. The child is then asked which glass contains the most liquid. The typical five-year-old will assert without hesitation that obviously there is more in the taller and narrower glass, and will readily demonstrate to you that this is the case since "the water is higher in this glass" or "now the water goes all the way up to here." Thus, for the five-year-old preoperational stage child, who seems preoccupied with a single dimension, in this case the height of the liquid in the glasses, the amount has actually changed. He is incapable of reasoning that the amount of liquid remained invariant (i.e., conserved) as a result of the transformation. The typical eight-year-old child, however, when confronted with this same problem will assert with the same degree of insistence that the amount of liquid has remained the same because "the new glass is higher, but the old one was wider." That is, the concrete operational child is capable of understanding the reciprocal compensation of the two dimensions of height and width, and thereby understands the concept of the conservation of amount.

It is primarily on the basis of these types of experimental observations, which Piaget has extended to include a wide range of concepts and dimensions, that he has argued for the reality of discrete stages in cognitive development. These stages appear to be characterized by very dramatic qualitative shifts in the form of the child's reasoning. The demonstrated shift from non-conservation in the preoperational child to conservation in the concrete operational child is particularly instructive in this regard since the latter child comes eventually to deny the validity of the answer he himself would have given during the former and earlier stage. Thus, for Piaget, cognitive development is *not* a simple process of the gradual acquisition of layers or accretions of knowledge, nor does it follow the model of cell proliferation, characteristic of physical growth. Rather, intellectual development is best viewed as an epigenetic phenomenon in which new cognitive structures, not present at an earlier age, emerge and undergo reorganization at each successive stage.

Before going on to a more detailed look at each of the specific stages Piaget has identified, several general points should be mentioned. Piaget has set out to write the ontogenetic history of cognition which for him largely represents the development of logical thought processes from birth to adulthood. The salient questions are ones such as: how does the child proceed toward an understanding of the concepts of object, space, time, and causality? How does he acquire those processes which make possible the conservation of length, area, and volume? How does he learn spatial and numerical relations? What are the origins of such logical acquisitions as the ability to understand the principles of classification, probability, and ordering a series, to name but a few? To the extent that these are the questions of most critical concern to Piaget, he is much more a student of knowledge than a student of children (Kessen, 1962), for whatever lies outside the cognitive domain is for the most part excluded. Although there are definite references in Piaget to the role of social interaction, play, identification, morality, these are in no way integrated to form a comprehensive picture of the personality development of the child. With these considerations as a background, each of the four major stages in Piaget's theory will be described briefly, highlighting only the critical features of each, and noting the most important implications for a general theory of development.[1]

Sensory-motor stage

The evidence for the development during this first stage, from approximately birth to two years, consists primarily of Piaget's very detailed and systematic observations of his own three children during their infancy (cf. Piaget, 1952; 1954). It is during this stage, which has a number of critical substages, that the infant begins his developmental journey from a reflexive to a reflective organism. He gains a rudimentary understanding of such basic concepts as space, time, and causality, largely because during this stage he establishes an awareness of the permanence of objects, and establishes a differentiation of himself from objects. Because the development of the object concept is such an important feature of this period, it will be highlighted in this brief description of the sensory-motor stage.

During the earliest months of infancy, reflex-schemas such as sucking, looking, listening, and grasping begin to undergo modification as a result of experience, and the most basic sensory-motor acquisitions or simple habits come into existence. According to Piaget, this general process begins when the infant *by chance* produces events which, because they are pleasurable or satisfying, are repeated.[2] These primary circular reactions, as Piaget terms them, tend first to be centered on the infant's own body, for example as in thumbsucking. During these early months, however, the infant's universe has no substantial permanence or spatial organization, and the major sensory-motor behaviors consist of the mere repetition or extension of the most recent fortuitous acts of accomodation.

Beginning somewhere around the third month there is a change in that the infant's reactions tend to be directed toward the manipulation of surrounding objects. Thus, when by accident he first produces a pleasurable effect such as striking a rattle and causing it to move, he will strike it repeatedly, attempting to maintain or reproduce the event. These repetitions directed toward objects or events in the infant's environment Piaget refers to as secondary circular reactions.

Shortly thereafter, one begins to see the beginnings of intentionality or goal-directed activity in the infant's primitive anticipation of finding an object just grasped. For example, if the infant drops the rattle, he will begin to grope for it in the immediate area. On the basis of such observations, Piaget would conclude that the infant is responding toward objects and events in his environment as if they possessed some permanence. Previous to this, such an object, if dropped outside the visual field was literally "out of sight, out of mind." However, it should be noted that at this particular substage there is no coordination between the visual and tactile systems, since the infant will not grasp at something that has disappeared from his visual field unless it has also been in contact with his hands shortly before.

It is not until somewhere around the eighth to the twelfth month that the coordination of the systems of vision and prehension is achieved. The infant's searching for objects becomes more purposeful, and he shows the beginnings of an appreciation of means-ends relationships. During this substage, he will actively search for an object which has been removed from his visual field; for example, if the rattle is placed under a sheet, he will remove the sheet in order to retrieve the rattle. However, he is not yet able to take account of a sequence of visible displacements. Thus, if the object is first hidden in position A, and subsequently hidden in position B, the infant will continue to search in position A.

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[1] For a complete review of both the theory and supporting research evidence, the reader is referred to Flavell, 1963, and to Hunt, 1961.

[2] Here Piaget does not concern himself with such issues at the heart of learning and behavior theory as the definition and role of rewarding or reinforcing events. His behavioral observations, most notably the repetitious nature of such behaviors, are sufficient for him to regard these actions as pleasurable or satisfying.

Piaget's observations have indicated that not until somewhere between the twelfth and eighteenth month is the infant able to conceive of displacement. At the same time, the infant also begins to experiment with new means-ends combinations. For example, he will extend the movements of grasping and searching to include a wider range of objects. At a slightly later substage, he attempts to vary this pattern of his response and discovers through this experimentation what variations he can produce in the environment. The repetitions of these clearly purposive acts Piaget terms tertiary circular reactions. The significance of this type of behavior is that the infant actively searches for or creates novel situations to which he can react, whereas previously his behavior changed only when he was forced to accomodate to an environmental demand.

During the final period of the sensory-motor stage, beginning somewhere around 18 months, the child begins to show some capacity for primitive symbolic representation. From the standpoint of the development of the object concept, the infant begins to develop an *image* of absent objects and their displacements. The child is now able to achieve solutions through a process of covert representational experimentation rather than overt trial and error sensory-motor explorations. An example from Piaget's observations illustrates the emergence of this new capacity: the child first watches you place a coin in your hand, then put your hand under a sheet, and finally bring your hand out empty. Rather than fumble around the area of your hand in search of the coin, or express bewilderment over the coin's whereabouts, the child reaches directly under the sheet in order to retrieve the coin. Thus, through representation, the child can "reconstruct" objects when the displacements are not visible, and can then direct his search by means of this representation. The laws of displacement have become dissociated from sensory-motor action itself, and rudimentary forms of deduction, a truly "intellectual" adaptation, begin to emerge. As Flavell (1963) describes this critical transition: "With the advent of the capacity to represent actions rather than simply to perform them, the sensory-motor period draws to a close and the child is ready for an analogous but even more extended and tortuous apprenticeship in the use of symbols [p. 121]."

The significance of the development of the object concept during this stage cannot be overemphasized. For concomitant with the infant's objectification of reality, he comes to view himself as an object among the world of objects, Prior to this, objects have not been dissociated from the few basic action schemas, e.g., grasping, looking, and sucking, which brought the infant into contact with them. Gradually, as the infant experiences objects in a variety of contexts, and they become associated with multiple and more complex schemas, they begin to emerge as objects distinct from his actions on them. Simultaneously, the boundaries between objects and self are becoming differentiated, and this represents what for Piaget is perhaps one of the most critical developmental steps, namely emergence from the infant's initial state of *egocentrism*. The meaning of this concept, so central to Piaget's thinking, is revealed in the following quote from *The Construction of Reality by the Child*:

> . . . it is precisely when the subject is most self-centered that he knows himself the least, and it is to the extent that he discovers himself that he places himself in the universe and constructs it by virtue of that fact. In other words, egocentrism signifies the absence of both self-perception and objectivity, whereas acquiring possession of the object as such is on a par with the acquisition of self-perception (Piaget, 1954, p. xii).

Stage of preoperational thought

During this stage, from approximately two to seven years, one sees the beginnings of symbolic thought, with language playing an increasingly important role. Thus, the child learns to distinguish between actual objects and the labels used to represent them; as a result, he gradually becomes able to reason symbolically rather than motorically, as in the sensory-motor period when he was limited to the pursuit of concrete goals of action. However, despite these very significant developments, the child is not able to perform those logical operations characteristic of more mature thought. For example, although the child has acquired the concept of the object, and may have a basic notion of certain classes of objects, his categories are based on but a single characteristic of the objects. He is still unable to classify a variety of characteristics simultaneously. Similarly, in dealing with physical objects and quantities, he is capable of attending to only one aspect or dimension, to the exclusion of others. An example of this type of prelogical reasoning was provided earlier in the description of Piaget's classic experiments on the child's judgment of the amount of liquid poured from one glass into a second taller and narrower glass. The preoperational child, focusing only on a single dimension, may conclude that after the transformation there is more water in the second glass because it is higher. Such thinking is dominated by the child's perceptions, and the salience of particular physical attributes. More importantly, it is characterized by the absence of one of the most important logical operations in Piaget's system, namely reversibility, i.e., the capacity to retrace conceptually a line of reasoning to its initial premise, or a series of displacements to its inital state.

At the preoperational stage, the child's reasoning is neither inductive nor deductive, but what Piaget terms "transductive." That is, he tends to relate the particular to the particular in an alogical manner. Thus if two objects or events are alike in one respect, they may be seen as similar in every respect. Events may be related not because of any inherent cause-effect relationship but simply on the basis of spatial or temporal juxtapositions. Furthermore, the child is unaware and therefore unconcerned about possible contradictions in his logic. It is as if he is unable, as Flavell (1963) has aptly described it, ". . . to treat his own thought processes as an object of thought . . . to reconstruct a chain of reasoning which he has just passed through; he thinks but he cannot think about his own thinking [p. 150]."

The prelogical thought during this stage takes several interesting forms which Piaget has documented extensively (1929). At the core of these cognitive processes is the young child's inability to clearly differentiate between self and the world, between the psychological realm of feelings and thoughts and the realm of objective reality and physical events. One form this takes is in what Piaget terms the child's "realism," for example, in his concept of dreams. Dreams are first conceptualized as external to the young child, as visible substantive events which occur outside him. Only at a much later stage does he come to the realization that dreams are the product of his own private thoughts and that this process is subjective and internal.

The child's inability to differentiate between psychological and physical realms can also be seen in the converse tendency to endow physical events and objects with such psychological attributes as consciousness, intention, and feeling. This form of thought has been labelled "animism." Here again, Piaget has documented a fascinating series of stages in which the child may first attribute consciousness and feeling to almost any object, particularly where there is movement involved. For example, a cup which is dropped to the floor may be described as "feeling hurt" by the fall. At a somewhat later stage, consciousness is only attributed to those objects which characteristically move, e.g., sailboats, clouds, etc. It is not until about the age of 10 or 11 that the child completely gives up such animistic notions and attributes consciousness and feeling solely to people and animals.

Piaget (1932) has also described how the child's prelogical notions of reality and causality influence his concepts of morality and justice. As Kolhberg has pointed out:

> Piaget believes that the cognitive limitations of the child of three to eight lead him to confuse moral rules with physical laws and to view rules as fixed external things, rather than as instruments of human purposes and values (1963, p. 395).

A good illustration of this characteristic pattern can be seen in Piaget's demonstrations of the preoperational child's view of "immanent justice," namely that punishment for wrong deeds is inevitable and inherent in the universe. This absolutism is further extended in the young child's judgment of the badness of an act in terms of its actual physical consequences.

All of these features type the preoperational child's representation and symbolic functioning as egocentric, in the sense that there is a relative lack of differentiation between the psychological realm of human experience and the objective world of reality. At this stage of development, the term "egocentrism" has definite social implications as well, for the young child is clearly the center of his own representational world. This characteristic is discernable in his inability to take the role or the point of view of another person, or to see things from a perspective other than his own. This is perhaps most obvious in his spatial representation of the world. For example, as Piaget's experiments have shown, the child at this stage is incapable of representing or describing a three-dimensional visual display of a landscape scene from any other spatial perspective than his own. The egocentrism of this period, then, is characterized by the child's pervasive but erroneous assumption that others share his limited frame of reference.

Through what Piaget terms the process of "decentering," the child learns during the preoperational stage to conceive of a spatial, temporal, and causal world of events which exists independent of himself. For this developmental transition to occur, the child must repeatedly experience social interactions in which his own point of view is challenged. Here, his play, his imitation of, and identification with, others, and the increasing use of language as a shared form of communication become important vehicles promoting this development. They repeatedly force the child to reevaluate his personal frame of reference, and to make the necessary changes or accomodations in his conceptualizations about the world of both physical and social events. Only in this manner does his childish egocentrism give way to a more objective view of reality. In considering Piaget's theory in its entirety, it is important to note that this is one of the few areas of behavioral development in which he is so emphatic, as well as specific, about the particular antecedent experiences necessary to promote this transition. While basic to his theory is the importance of the developing organism's encounters with the environment, rarely in his observational accounts does Piaget spell out the precise nature of these encounters nor how they interact to produce the cognitive behavior he describes.

The stage of concrete operations

This third major stage, from approximately age seven to eleven, represents a critical step in the developmental progression characterized by the emergence of increasingly more internalized symbolic functioning (see Inhelder and Piaget, 1958). It is during this stage that the child becomes capable of reasoning with what can be called logical operations. Furthermore, these logical thought processes become coherently organized into a complex and integrated network with which the child confronts and systematically responds to the world around him. The key to appreciating the dramatic developmental accomplishments of this stage lies in an understanding of the term "operation," the cognitive schemas of more mature thought. In its most general usage, an operation refers to a symbolic or representational act which is part of an organized conceptual framework. More specifically, it refers to such numerical operations as addition, subtraction, multiplication, division, and to such logical processes as classification, ordering, etc. As a guideline, Piaget has suggested that actions which can be represented by such common mathematical symbols as $+$, $-$, $\times$, $\div$, $=$, $<$, $>$, to illustrate a few, be viewed as intellectual operations, though this by no means constitutes an exhaustive list (Flavell, 1963).

One important characteristic of an operation is that it is reversible. To cite an example from the realm of numerical concepts, the child can reverse the operation "four times two is eight" by performing the operation "eight divided by two is four." This same characteristic of reversibility holds true for such logico-deductive principles as transitivity, i.e., if $A < B$, and $B < C$, then $A < C$. The reversibility of operations is also a prerequisite for an awareness that certain properties of objects are invariant, even though they may undergo certain transformations. The concept of conservation, one of the most thoroughly studied reversible operations in Piaget's system, is best illustrated in the experiments on children's judgments of the relative amounts of liquid contained after a series of displacements to glasses of differing dimensions.

The concrete operational child is capable of performing such reversible operations, and during this period organizes them into an increasingly integrated cognitive system. It is not merely the emergence of the ability to perform such operations on a broadening range of objects and events which highlights the cognitive change during this stage, but the fact that these intellectual operations become solidly, coherently, and adaptively organized. For Piaget, the basic qualities of organization and adaptation are of paramount importance in determining the course of intellectual development. As noted earlier, Piaget's primary interest in charting the ontogenetic changes in cognitive development is the isolation and description of the structural changes in the organization of intellectual processes at the different stages. This is perhaps nowhere illustrated quite as dramatically as in the shift from preoperational to logical operational thinking.

The child of the concrete operations stage does not represent the end-point in this developmental progression, however, since as the very name of the stage implies, the application of these operations is not yet dissociated from the concrete objects and events in the immediate environment to which they apply. Therein lies the cognitive limitation of this period, for there is not yet a system of formal logic which is completely divorced from its subject matter. For example, during the concrete operations period, the operation of conservation does not emerge full-blown and equally available for application to any realm of events but undergoes the following progression: conservation of matter or mass, then weight, and finally volume toward the end of this stage. What the child is learning, however, is that thought is a more trustworthy guide to his actions than is perception. It is not until the final stage of cognitive development that logical operations can be performed independent of and in the absence of the concrete world which fostered their emergence.

Another important aspect of the concrete operations period which deserves mention is the fact that the operations which characterize this stage are not only applied to the realm of objects, numbers, time, and space, but also to the realm of social relationships. For example, the child's value structure, including codes of conduct, and views of moral obligation and necessity reflect the same principles which are pervasively evident in every realm of the child's cognitive functioning. As Flavell (1963) points out:

> In Piaget's view it is no accident that the child, of, say, ten years is beginning to develop a hierarchy of values and well-ordered systems of beliefs about rules and laws, mutual obligations among peers, and the like (1932) ; he has developed cognitive structures which make these things possible—possible at ten and not possible at four. What happens in what might loosely be called "extra-cognitive adaptation" is at any age very much dependent upon the nature of the cognitive organization so far developed, and therefore the study of the latter is of prime importance for students of personality . . . [p. 82].

Piaget's studies of the child's changing conception of rules during this stage provides a good illustration of this point. In observing and questioning children about the game of marbles, for example, Piaget (1932) discovered that prior to the concrete operational stage, children regard the rules as absolute and unchangeable having been handed down from either parental or divine authority. However, an interesting discrepancy exists between the young child's avowed concept of rules and his performance, since his own egocentrism makes it difficult for him to adhere to these inviolable laws in his actual game-playing. It is not until the end of the concrete operations period that the child fully appreciates the origins of rules, as well as their social function. When this understanding is achieved, rules may then be changed, provided there is a consensus among the players; once agreed upon, however, they must be rigidly adhered to in practice until such time as there is a formal agreement among all participants that further change is necessary or desirable.

In his general description of the concrete operations stage, Piaget has emphasized the child's cognitive efforts to organize, integrate, and articulate his representational world. This feature is particularly obvious in the child's attitudes toward rules. Toward the end of this stage, the rule systems become increasingly complex, and serve an increasingly important function in the social organization of the child's world. Many of the games during this period take on ritualistic proportions in terms of the investment in codification, revision, and elaboration of rules. In this realm of behavior, as with every other, the defining characteristic of the stage prevails, namely the child's attempt to impose structure and organization on the real world of objects and events.

Stage of formal operations

During this period, from approximately 11 to 15 years, the child, on his way to becoming an adolescent, overcomes the intellectual limitations of the preceding stage. Thus, for the first time, he becomes able to take the final steps toward reasoning with abstract, rather than concrete, concepts and relationships. He is able to grasp the structure and meaning of a logical proposition or argument, independent of its specific content. Unlike the concreate operational child whose concern is the organization and ordering of concrete objects and events in the immediate environment, the formal operational child turns his attention to the potential instead of the real. This emerging preoccupation with the hypothetical is one of the most significant features of this period (Inhelder & Piaget, 1958). Armed with the intellectual ability to create hypotheses and deduce logical conclusions, his problem-solving is now characterized by a procedure of first envisaging the myriad possible relationships which exist; then, gradually, through a systematic process of logical experimentation and deduction, he arrives at the appropriate solution or proof. In such a cognitive scheme, reality becomes merely a unique subclass within the broader class of the hypothetically possible (Flavell, 1963).

It is not simply the ability to reason according to this hypothetico-deductive method which is the distinctive advance during this period, but also the fact that the approach becomes a pervasive style of problem-solving. As Flavell notes, it amounts to a fundamental reorientation toward cognitive problems. He goes on to point out:

> No longer exclusively preoccupied with the sober business of trying to stabilize and organize just what comes directly to the senses, the adolescent has, through this new orientation, the potentiality of imagining all that might be there—both the very obvious and the very subtle—and thereby of much better insuring the finding of all that is there (Flavell, 1963, p. 205).

In the writing of Piaget and his colleagues, most notably Inhelder and Piaget (1958), those characteristics of formal thought which constitute the intellectual armamentarium of the adolescent are spelled out in detail. Any adequate discussion of these logical operations, particularly those which are described in the language of mathematics and the notation of symbolic logic, is beyond the scope of this article. However, several general characteristics deserve brief mention. In addition to the hypothetico-deductive nature of the adolescent's thought processes, his reasoning follows the pattern of propositional thinking. Hypotheses and deductions are expressed in linguistic formulations containing propositions, for example of the "if . . . then" type. Thus, logical operations are performed on statements or assertions about particular events, rather than directly on the events themselves.

The method of "combinatorial analysis" is also available to the adolescent during the formal operations stage. That is, in a problem-solving situation he is able to isolate individual variables as well as all possible combinations of variables which might be responsible for any particular cause-effect relationship. This is illustrated by a series of experiments (Inhelder & Piaget, 1958) in which the child is presented with a number of beakers. Each beaker contains a colorless liquid with certain chemical properties which will cause it to change to a particular color if mixed with one or some combination of the other liquids present. When confronted with the problem of producing a particular color designated by the experimenter, the formal operational child goes about this task in a very orderly and systematic manner. He successively rules out each of the finite number of possible combinations of the available liquids which might hypothetically produce the desired color. While the approach of the concrete operational child cannot be classified as entirely haphazard or disorganized, it is incomplete, unsystematic, and generally unsuccessful.

One additional set of operations which becomes elaborated during this period includes those transformations which make possible such complex logical and mathematical concepts as probability. Propositional algebraic structures are also developed during adolescence, as is the ability to perform calculus. Piaget places heavy emphasis on these mathematical acquisitions, charting the developmental sequence of these operations more thoroughly than perhaps any other in the system. On this issue students of Piaget have often been critical of what appears to be his total immersion into formal mathematical theory which has led to a rather one-sided picture of adolescent development.

Although such criticisms are to a large extent justified, nevertheless in one of their more recent descriptions of this period (Inhelder & Piaget, 1958) the authors do conclude with a brief excursion into the implications of the adolescent's newfound cognitive abilities for his personal and social behavior. The most significant implications would seem to stem from his preoccupation with the hypothetical. Flavell cogently paraphrases Inhelder and Piaget when he states of the adolescent:

> His conceptual world is full of informal theories about self and life, full of plans for his and society's future, in short, full of ideation which goes far beyond his immediate situation, current interpersonal dealings, and so on . . . . The adolescent is beginning to take up adult roles; for him the world of personally relevant future possibilities—occupational selection, marital choice, and the like—is a most important object of reflection (Flavell, 1963, p. 223).

Implications

In their concluding remarks about the growth of logical thinking from childhood to adolescence, Inhelder and Piaget (1958) point out the important relationship between the cognitive processes available to the adolescent and the activities and concerns in his everyday world. For the concrete operational child as well, a similar parallel exists between level of cognitive development and the concepts making up his social, moral, and value structure (Kohlberg, 1963; Piaget, 1932). However, Piaget does little more than suggest those areas of application where a knowledge of the particular cognitive processes defining each developmental stage may enhance our understanding of the child's social and personal adjustment. As mentioned at the outset, Piaget is, above all, a student of knowledge, whose primary concern is the ontogenetic evolution of logical thought processes.

Piaget's emphasis on the structural features of the child's changing cognitive system is largely independent of the particular dynamic content to which these processes may be applied. Even when he deals with the child's changing concepts in such areas as moral development, Piaget is interested in the formal features of these thought processes. As Kohlberg (1963) notes, Piaget's account of moral development is derived primarily from his general theory of the development of the child's concept of the world. Consider, for example, the young child's view of "immanent justice," namely that punishment for wrong deeds is inevitable and inherent in the universe. Here Piaget's focus is on the cognitive processes with which the child conceptualizes this contingency, rather than the content of the particular misdeeds or their punitive consequences.[3]

Related to Piaget's general lack of interest in the dynamic content of thought is his relative unconcern with emotional development. For example, Piaget's treatment of the development of moral judgment does not deal with such issues as the role of guilt feelings, anxiety, and related considerations generally treated under discussions of conscience and super-ego development. Furthermore, he does not deal with questions concerning the antecedent conditions which may promote or motivate acts of transgression, nor does he concern himself with the affective or emotional consequences for the child.

Piaget's analysis of development does overlap with the more psychodynamic Freudian approaches in those areas which have been described in the psychoanalytic literature as "conflict-free spheres" of ego development. Neo-Freudians in particular have employed this term to describe such ego-functions as locomotion, perception, memory, problem-solving and language, the development of which is not viewed simply as a consequence of conflict between instinctual need and frustrating reality. In the psychoanalytic scheme, such egofunctions take on an autonomy similar to the intrinsically-motivated functioning of the behaviors described by Piaget. However, it is here that the two positions diverge, to the extent that each views such behaviors within a different frame of reference, with differing degrees of emphasis. The more psychodynamic approaches integrate the role of ego functions with other aspects of behavior, to form a total picture of the personality development of the child. As has been emphasized, Piaget is relatively unconcerned with emotional, social, and personality development, per se.

Nevertheless, Piaget's theory contains definite implications for the study of personality development, some of which are of clinical significance. In large part, these implications stem from Piaget's elucidation of the illogical, or prelogical, nature of the young child's thinking. The resulting distortions of reality in the realm of time, space, objects, and events have been the major focus of Piaget's efforts, however, these same principles may be applied to the realm of social and interpersonal relationships as well. One important feature of the preoperational period is the child's frequent inability to distinguish clearly what he imagines from what he recalls, namely his frequent confusion between fantasy and fact.

Within the context of these preoperational cognitive limitations, one may consider the Freudian concept of the Oedipal conflict, which is viewed as central to the psychosexual development of the young child. Concomitant with the strong emotional attachment to the parent of the opposite sex are fantasies about the future of this relationship. One frequent form that these fantasies take is the wish to marry the parent; even more significant from the standpoint of the child's level of cognitive development is his illusion that this may, in fact, be possible. Thus, it is not only his intense emotional needs but his firm conviction as to the outcome of this relationship that makes this period one of the most complexly significant struggles of the child's life. Magical and inconsistent thinking permeates his fantasies about sexuality, his views about parental intercourse, his castration anxiety, as well as his fear of, and wish to identify with, the parent of the same sex. In the mind of the prelogical child, these beliefs have an overwhelming reality.

A more direct clinical application of Piaget's theory has been noted by Woodward (1965) in reference to the reaction of young children who have been hospitalized for an operation or illness. Drawing upon data contained in a study by Prugh et. al. (1953), Woodward writes:

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[3] The reader is referred to the excellent work of Kohlberg (1963) who has reviewed and extended Piaget's work on moral development, integrating it with other research in this area.

> The tendency of the 6-8 year old children in this study to regard their illness as a magical retribution for their bad behavior is in accord with Piaget's results on the concepts of the world and the moral judgments of children of this age (p. 81).

Woodward also notes that the most marked emotional reactions occurred in those children aged 2-4 who were strongly attached to the mother. This she attributes to the combination of their strong emotional tie, in conjunction with their cognitive inability to understand the conditions under which they were hospitalized, specifically the mother's promise that they would return to her care at home. Piaget's theory provides valuable normative guidelines for how the child may *interpret* or conceptualize such events. However, as noted earlier, his theory does not speak to the issue of either the affective or cognitive consequences of these experiences for the child. Here, clinical research, particularly in the form of long-term follow-up studies of such children, is badly needed.

Another example of the fruitful way in which psychodynamic and cognitive considerations can be integrated to provide a more comprehensive picture of behavioral development can be seen in considering the stage of adolescence. The concerns typically viewed as central during this period are the upsurge of genital sexuality, social relationships, problems of identity, independence, and impending adulthood. The Piagetian analysis of the developmental accomplishments during this period adds a new perspective to our understanding of the adolescent, namely the intellectual capacities available to him whereby he can conceptualize the problems confronting him. Piaget's delineation of the cognitive processes which emerge during this period would appear to be restricted to various logical and scientific problem-solving situations. While the examples upon which he draws are certainly based upon experimental evidence of this nature, his concern with the general characteristics of these processes highlights their applicability to many areas of adolescent functioning. As pointed out in the description of the stage of formal operations, the preoccupation of the adolescent with hypothetical events is a critical feature of this period. When one considers this observation in light of the more psychodynamic descriptions of adolescent concerns, one begins to see the value of such an integrated approach to development. No realistic understanding of this period can be gained unless we know not only the formal cognitive processes available, but also the areas of content and personal concern to which they are applied, and why.

One can also see in Piaget's theory the implications for a better understanding of psychopathology. For example, his description of the intellectual achievements of the formal operations period, the ultimate stage of cognitive development which characterizes adolescent and finally adult functioning, has implications for that important feature distinguishing normal from pathological adjustment, namely appropriate reality testing. In describing this stage Piaget merely *informs* us of the adolescent's preoccupation with the hypothetical. However, it would seem that the ability to conceptualize myriad hypothetical situations and to entertain various abstract possibilities about whatever life events are most salient might represent something of a double-edged sword. There is no guarantee, for example, that the adolescent will be motivated to employ the logical ability to distinguish the real from the unreal in pursuit of that intellectual goal. The opportunities to engage in ruminative fantasy may also lead to intricate distortions of reality which are pathological in nature, and may provide a guide to more overt abnormal behavior. One sees in Piaget's theory certain implications for the very complex intrapsychic life displayed by the adolescent, as compared to the younger child at less mature stages of cognitive development. However, Piaget's observations only take on such meaning when considered in the context of their motivational, emotional, and social significance.

Although Piaget is relatively uninterested in pathological behavior per se, his descriptive data have been shown to complement the evidence supporting the Freudian model of fixation at, and subsequent regression to, particular stages of psychosexual development. This application is most evident in considering the various forms of psychosis, all of which are characterized by loss of contact with reality and the predominance of illogical thought processes. One specific example, out of many, can be seen in such schizophrenic reactions as object estrangement and depersonalization. In psychoanalytic terms, these psychic phenomena represent a regression to the oral stage, in which problems relating to the differentiation of self and environment are revived, and there is a loss of one's sense of identity and the separateness of other people, objects, and events. Here one can see the relevance of Piaget's observations of the egocentrism displayed during the sensory-motor period, an egocentrism which is characterized by lack of differentiation between self and world, namely the "absence of both self-perception and objectivity" (Piaget, 1954, p. xii).

One reason why there has been so little in Piaget of direct relevance to questions of abnormal or deviant behavior is the fact that for the most part he has been uninterested in the problem of individual differences in rate of development. His focal point has been the demonstration of the sequentiality of stages, independent of the precise age at which they are attained. The fact that different children may pass through these stages at faster or slower rates is in no way damaging to the theory, as Piaget has formulated it. However, this issue is certainly of critical significance to many students of child behavior who demand an explanation of this fact from a theory of development.

Stated somewhat more directly, Piaget has been relatively uninterested in identifying those antecedent variables which accelerate or retard the rate of cognitive development. Like many developmental frames of reference, his emphasis is on the observation and description of lawful behavioral changes per se, rather than the illumination of the particular causes of this developmental progression. While he certainly stresses the role of experience as essential to cognitive change, environmental encounters are viewed as catalytic to this process, rather than as specific events or experiences to be assimilated or learned.

The issue of the role of specific experiences is of no small significance, particularly in view of recent renewed interest in educational training programs designed to offset the progressive retardation observed in those children who have been identified as the culturally "deprived" or "disadvantaged." The rationale for such intervention programs is derived, in part, from recent research, mostly in animal literature, demonstrating the significant long-lasting effects of early experience. Such spokesmen as Hunt (1961) also draw heavily on Piaget's body of theory and observations in support of such early enrichment programs. However, these efforts represent something of an extrapolation from Piaget's model of development in that he does not assert that rate of development can be altered dramatically, nor does he delineate what specific experiences or type of training might be necessary in order to do so. In his most recent writings, however, Piaget has directed more attention to this general problem. He has asserted that intellectual growth is a function of the variety as well as the degree of stimulation, and that such growth can be accelerated to some extent under optimal conditions of stimulation. He goes on to qualify this general principle in noting that there is a maturational component involved, such that the child must be within the critical period of maturational readiness in order for the organization and development of cognitive skills to occur. However, just what factors control maturational readiness, and what specific types of experience promote development of this sort remains as yet unclear. Thus, this very timely issue contains many intriguing questions for further research in an area of both scientific and practical concern.

In conclusion, Piaget's prodigious and systematic body of work has had a profound influence on the entire field of child psychology. His penetrating observations and fresh insights into the nature of child development have stimulated more research during the past decade than any other single person in the area. As Flavell (1963) has noted of Piaget's contributions, he has charted the ontogenetic course of such concepts as space, causality, time, etc., for which we had no reason in our years of child observing to expect a developmental history. More importantly he has ordered these observational data into a systematic stage-analytic theory of cognitive development which is the most comprehensive one of its kind in existence. This article has only hinted at the scope as well as the detail of his efforts in this direction.[4] Cleary, Piaget has given us a compelling and provocative look at how the phenomenological world of the infant becomes the world of the child, the adolescent, and finally the adult.

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[4] Discussions of the research generated by Piaget's formulations, as well as critiques of his position, can be found in Flavell (1963); Hunt (1961); Kessen & Kuhlman (1962); Sigel (1964); and Zigler (1963).

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Genetic Information Center
Connecticut State Department Of Health

The Connecticut State Department of Health announces the establishment of a Genetic Information Center.

Diseases and disabilities with a genetic etiology are being seen with increasing frequency. The medical practitioner who has been concerned with acute and chronic illnesses is finding himself called upon on occasion to treat genetic disorders and to counsel prospective parents about genetic disorders for which information is not readily available to him.

The Genetic Information Center offers direct consultation to the medical practitioner. It will provide him with information on the inheritance of the disorder of concern so that he in turn can counsel the patient on the risks and implications to himself and his family. It will maintain an inventory of diagnostic and treatment facilities in Connecticut and neighboring states. The Genetic Information Center is a resource for physicians, to whom it will furnish needed information or makes referrals to suitable experts in the field.

The Genetic Information Center shall be guided in its endeavors by an advisory committee consisting of:

Stewart Seigle, M.D. Chairman, Internist, 85 Jefferson Street, Hartford

W. Roy Breg, M.D., Senior Physician, Southbury Training School

Ira Gabrielson, M.D., Assistant Professor of Public Health and Pediatrics, Yale University School of Medicine

Merton S. Honeyman, Ph.D., Director of Program Analysis and Research, Office of Mental Retardation, State Department of Health

Herbert Lubs, M.D., Assistant Professor of Medicine and Pediatrics, Yale University School of Medicine

Howard Wetstone, M.D., Assistance Director, Department of Medicine, Hartford Hospital

All inquiries should be directed to:

Merton S. Honeyman, Ph.D., Director
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State Department of Health
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Birth Defects and the Psychological Development of the Child: Some Implications for Management

A. Herbert Schwartz, M.D. and Julius Landwirth, M.D.

Comprehensive care of the child with a congenital deformity should begin prior to the birth of the child. Each woman during her pregnancy asks herself questions, which begin, "what if?" Some questions concern congenital defects. Being pregnant increases her interest in facts about pregnancy, birth, and child rearing. Friends and relatives funnel to her both old and new information. Recently the lay press has widely publicized such considerations, including articles on the newly discovered intrauterine hazards. Today, the expectant woman is frequently stimulated beyond her normative concerns to consider the possibilities of abnormalities in her child.

How the expectant mother copes with these questions is based not only on her personality and on her prior experience with defects but also on her relationship to her parents, husband, and physician. Support in coping with the initial fears evoked by such questions and the opportunity to clarify them with husband, significant relative, or friend and physician are important determinants of how she will respond to the birth of a deformed child.

The aim of this paper is to provide information which may help the physician prevent secondary complications of birth defects i.e. social and emotional handicaps. This paper will also integrate to a significant extent knowledge of child development with the scant data on the effect of some congenital defects on the development of the child's personality.[1] This paper does not attempt to provide specific references to all defects. Noticeably omitted are mental retardation, cerebral palsy, and other neurological defects. However, the principle conceptualizations derived from our studies are relevant to all defects.

Public Reactions

The public attitude of accepting the congenitally handicapped frequently masks a deeper feeling of abhorrence or repugnance. This surface acceptance and underlying revulsion results in the over compensatory behavior which denies the impact of the defect through the all too sweet, all too attentive and all too permissive response. Gudmund Harlem, M.D., Minister of the Royal Norwegian Ministry of Health and Social Affairs, illustrated one of the stereotypes in action when he spoke to the International Society for the Welfare of Cripples.

> "A girl I once met told me this little story: She had been crossing the Atlantic on one of the big liners. Her age was around 20. She shared a room with a sweet and friendly lady around 50. The young girl had a one-sided below the knee amputation but was not very much bothered from a practical point of view by her prosthesis. The young girl did not return to the cabin until rather late and her roomate asked her "why are you so late?" "What does a one-legged girl do this time of night?" She answered, "well, what does a two-legged girl do?" "Oh, you don't do that, do you?" was the reaction of the old lady.
>
> We may smile at a little story like this one, but we should also regard its serious implications. The girl had been completely rehabilitated. All our technical knowledge had been put to use. She had received the full degree of independence of her disability which we as rehabilitation workers knew how to achieve, but what we did not achieve was to change the attitude of her fellow man."[2]

The belief that a warped body means a warped mind is deeply rooted in the public unconscious. This concept, personified in such literary characters as Long John Silver, Captain Hook, Captain Ahab, and others, is epitomized in Shakespeare's Richard the Third:

But I, that am not shaped for sportive tricks,
Nor made to court an amorous looking glass;
I, but am rudely stamped and want love's majesty

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to strut before a wantom ambling nymph;
I but am curtailed of this fair proportion,
Cheated of feature by dissembling nature
Deformed, unfinished, sent before my time
Into this grieving world, scarce half made up,
And that so lamely and unfashionable
That dogs bark at me as I halt by them;
. . . since I cannot prove a lover,
To entertain these fairwell spoken days,
I am determined to prove villain
And hate the idle pleasure of these days.

Parental Reactions

The development of the child's personality is critically derived in the context of the parent-child relationship. Therefore parental reactions are crucial influences on the child's optimal development. Similarly the child's development crucially influences the parents' mental health.

The birth of a child with a deformity is often considered in psychological terms as a loss.[3 4] As such, the loss of the mother's and father's expectations for a healthy child evokes a mourning reaction similar to the reactions associated with the loss of a loved one. Through the process of mourning their anticipatory fantasies and goals attached to the potentially healthy infant are given up and each parent must then develop new goals adjusted to the changed realities and potentialities of the child that was born.[3 4 5] Despite the physician's help in guiding the parents through the acute phases of the mourning reaction and its resolution over a 6 to 12 month period the parents may experience an intermittent reawakening of this reaction. Frequently, at each of the successive developmental crises the feelings and behavior associated with the mourning process are worked through again.

> Mrs. V. a college educated mother whose 5 year old boy was about to enter kindergarten after a successful nursery school experience sought psychiatric consultation. At age 4 an extensive evaluation performed by an outstanding physican whom the mother and father both highly regarded found that this child was perhaps of average endowment while his two siblings were of superior intelligence. No birth defects nor neurological dysfunctions were determined. The mother continued to insist that because the birth of the baby "was delayed" a few moments a neurological defect occurred which now made this child develop more slowly. She believed that the defect accounted for his immaturity, his inability to play with peers (not documented by the nursery school report) and to have what his mother discribed as "a cloud in his mind."
>
> During the course of several interviews with Mrs. V. her sadness, withdrawal, resentment, self-blame and her need to prolong the infantile ties to this boy became apparent. The mother described her current feelings as similar to those she experienced after his birth and again when he began nursery school.
>
> Although this case does not describe what physicians might most frequently consider a child with a birth defect, to this mother her child's average development and average intellectual abilities when compared to her other children confirmed her belief that this child had a defect. At each stressful event, she re-experienced successive episodes of feelings associated with a mourning reaction.

In this case as in many others the pitfalls of an inadequate resolution of the mourning reaction are expressed repeatedly throughout the child's development. Frequently feelings of rejection, shame, over-protectiveness, over-solicitude, and overdemand in areas of development not directly affected by the defect may be the residues of an incompletely resolved mourning reaction.

Developmental Reactions

Though the child has a mal-formed body he continues to proceed through maturational stages specific for the human species. Throughout this development there is a continuous adaptation to the physical defect. A man with one arm may develop it to an extraordinary adeptness or in a like manner, the blind child may develop an exceptional sense of smell or hearing. Similarly, the personality continues to mature through stages of development adapting to the maturation of the body,[6] to the changing awareness of the physical defect and to the parental and public attitudes towards this defect. Just as physical adaptation is more prominent during critical stages of physical development so too psychological adaptation will be more in evidence during critical psychological stages. These dynamic processes, the physical and the psychological are concurrent and interwoven. Successes or failures may be mutually potentiated in either a positive or negative manner.

> James, a 5 year old, with a partial absence of his right upper limb, attempted to participate in all activities in his pre-kindergarten school. Despite much help and support from his teachers, his participation in certain activities

remained limited. The more frustrated he became the more aggressive he behaved. Soon his peers began to dislike him, he became destructive. Concomittantly, his willingness to participate even in areas in which he was capable decreased.

For James the psychological adaptation to his handicap necessary for interaction with his peers was not successful and deterred the progress of his physical abilities.

Each successive stage of personality development emerges from the patterns of development of the previous stages.[7] [8] [9] Therefore difficulty in any one phase of psychological development affects subsequent phases.

In early infancy the child explores his environment with his eyes, ears, mouth and hands. Deformities in any one of these parts will alter the methods by which he attempts to succeed in this developmental task.[10] Various congential neurological dysfunctions may interfere with attempts to acquire motor control and patterns such as eye-handedness, equilibrium, and rhythms of rest and activity. The child's early awareness of himself as an individual with a particular body image is influenced by the impact of a physical defect. In early infancy the child's major developmental task is the acquisition of a sense of trust in himself and his environment through a satisfactory mothering experience.[8]

The child with a cleft palate experiences a prolonged inhibition of sucking activity which may later contribute to speech difficulties. The cleft palate may also cause feeding difficulties which decrease both the mother's pleasure in feeding her child and the child's pleasure in being fed.[11] These attitudes toward feeding experiences are significant in shaping the child-mother relationship.[12] The child's conflicts and hardships in achieving satisfaction in feeding experiences and the frustration of the mother's need to nurture comfortably and successfully enhance the stress already placed on their relationship by the birth of a child with a defect.

Frequently the mother's anxiety and guilt become overwhelming and she partially withdraws from the mothering task. Occasionally the defect and its care interfere with cuddling, an essential component of adequate mothering. Often, frequent hospitalizations are necessary and adequate stimulation, affection and continuity of care are not maintained. These factors may affect the mother-child relationship to a degree which will alter the foundations of personality development—the child's sense of trust. Although alterations in the early mother-child relationship in children with congenital deformities have not been closely correlated with specific future personality characteristics the major influences of these early relationships are well known. The affects of emotional deprivation have been repeatedly documented.[13-17]

In the second or third years, late infancy, the developmental tasks of increased independence may be delayed because of sensory defect, malformed extremities, or over-protectiveness. The child's need to adjust to authority and to limit setting can be hampered by the parents' inability to set well defined limits because of unresolved feelings of guilt. The child with congenital heart disease benefits, as do all children, from parental control and limit setting. But the parents of these children already uncertain of themselves find the area of discipline to be magnified as a source of anxiety, uncertainty, and guilt. Often they are unable to carry out everyday training measures which they have used comfortably with their other children.[18] Poor adjustment and anxiety in the cardiac child often seems more related to maternal anxiety and pampering than to the incapacity.[19]

In children with genital or anal defects, toilet training may become a scene of intense conflict. Toilet training necessitates the use of the deformed body part and provides parents with a constant reminder of their child's defect. Whether or not the child is ready to control his elimination may be more difficult to answer. Because of the parents' and often the physician's uncertainty, the child is frequently presented with ambiguous expectations. Children with imperforate anus frequently have poor bowel control for several years. Often when the parents are unaware of this or are unable to tolerate it they involve themselves in a conflict with their child. The urinary function of boys with genital hypospadius is a focus of anxiety from birth. The parents' initial doubt as to his ability to urinate sufficiently may have been resolved but they are now faced with new questions—can he control his urination or is there some further defect? In severe cases where the urethra opens onto the perineum, boys must sit to urinate. Frequently they find their mode of urination unacceptable because they are unable to stand like daddy. To stand to urinate is a salient part of the early imitation of father and later masculine identifications. In all genital defects parents are concerned whether their child will be sexually competent and able to pro-create. Despite the physician's answers, significant doubt may continue to exist and may alter their expectations of this child.

The certainty and security of sexual identity is a cardinal factor in personality development. In children with ambiguous genitalia, a delay in gender identification after the second or third years may produce an excess of inhibitory and control functions in the personality.[20] Periodic depression, sullen and anxious bashfulness, and extreme but circumscribed diffidence and guardedness pertaining to sexual situations have been described.[20] However even when fully aware of a baby's genital ambiguity parents do assign one sex or the other. They cannot wait indefinitely before announcing the birth of a son or daughter. Furthermore language dictates that that they refer to the child as he or she. Later attempts to change such assignments on the basis of more scientific data may conflict with a gender role which for the most part is already fixed.[21] [22] (Salient considerations in management are discussed in the references cited. It is outside the more general scope of this paper to discuss the management of any one congenital defect in great detail.)

In late infancy the child begins to acquire feelings of adequacy or inferiority and of being physically intact or defective. He experiences feelings about other people—are they trustworthy, lovable, or hostile? If the parent-child attitudes are marked by continued rejection, shame and over-protection the child will not experience normal relationships with siblings, peers and adults.

Critical to this stage of development is the growth of a sense of autonomy. This sense of autonomy and with it the resolution of the expected ambivalences of love and hate, cooperativeness and willfulness, self expression and renunciation may be marred by a sense of shame and doubt.

In the third to sixth years, early childhood, the child is expected to develop an increasing ability to take directions, to be obedient, to interact with peers, and to experience a rapid growth of language and concept formation. He increasingly accepts his own sex and his own sex role. This is a critical period for developing healthy attitudes toward sex. There is a further development of conscience and an acquisition of an acceptable degree of initiative.

In children with idiopathic sexual precocity, there may be marked muscular development and an increase in aggressive behavior. These combined with physically appearing older lead to a parental reaction that fosters over control and inhibition.[23] [24] School acceleration of these children must be seriously considered though the IQ may be only average.[25] On the other hand, children with short stature are frequently treated according to their appearance of being younger and less demands may be made upon them for continued development. Because of their differences their ability to interact and compete with their peers may be curtailed. Children with dwarfism have a conspicuous deficit of personality traits associated with aggressive mastery and with destructive behavior. Few instances are reported in these children of temper tantrums, destructive acting out as in fire-setting or stealing and none of assault or social delinquency.[26]

All children with defects may begin to experience inappropriate feelings of responsibility and guilt for their deformity.[27] Such feelings may produce overwhelming anxieties and a diminished ability to interact with peers.

> James, a six year old boy, during his hospitalization for an evaluation of his short stature attributed his growth problem to the following causes. "Maybe because I was the last born and I got my mother sick. (a post partum depression) Maybe it's because I don't eat peas." In both these explanations he was quite serious and it was difficult to dissuade him from these beliefs. In addition, James was passive, usually sad-faced and rarely complained when receiving the numerous needle punctures necessary for this evaluation. The nurses never observed him to be angry and when threatened by another child or deprived of attention he would quietly retreat, rather than strike out, or actively compete.

In late childhood, from six to puberty, the child involves himself in the formation of peer groups. He identifies with contemporatries of the same sex, refines and elaborates small muscle skills, and learns realistic ways of controlling the physical world. He uses language to exchange ideas and influence people. He begins to free himself from primary emotional dependence on his parents. He learns to give as well as receive love. He acquires a repetorie of social rules that he uses in the service of socializing and develops a sense of morality. It is a critical stage for acquiring a sense of duty and accomplishment. The tasks associated with this stage are school adjustment, social relationship, feelings of adequacy, and sexual understanding.

In late childhood, how the child sees himself becomes more firmly established. His body image is shaped by sensory perceptions in conjunction with environmental response to the body and its defects. The clarity and stability of this image exerts an essential influence on mental functions; a serious distortion of this image will manifest itself in the impairment of mental functions. Occasionally, thinking, learning, and memory are impaired.

Children with crytorchidism frequently exhibit typical symptoms. These children have been described as hyperactive, accident prone, socially inadequate, and having a learning difficulty. Also they have been characterized as having a tendency to exaggerate, to lie and to fantasy. Cryptorchidism is not considered the primary pathogenic factor, but the way the parents, particularly the mother, experiences the congenital defect accounts for the child's preoccupation with his testes and his symptomatology. A drastic diminution of symptoms occurs once the intactness of the genitals is established.[28]

Defects that are not so readily corrected appear to be related to other factors that influence school performance. In dwarfs, although physical retardation is not paralleled by mental retardation, early school achievement is unsatisfactory and does not correlate with intellectual ability. In many of these children a continuous search for approval from their peers and their teacher interferes with their school work.[29] Intellectual development of children with congenital heart disease as measured by intelligence testing is delayed. This difference appears to be a consequence of a lack of schooling, easy fatiguability and an emotional disturbance.[30]

In late childhood the personality responses to a deformity may pass beyond a temporary psychological reaction and become incorporated as an integral part of the personality. Even if the defect is repaired the child may react as if the defect still persists.

> Tony, an 8 year old boy, was referred for psychiatric evaluation with the complaint of aggressive and provocative behavior within the classroom and at home. A final repair for the cleft palate had taken place 9 months prior to the referral. Three months prior to the consultation the family had moved from the city to a suburban middle class community. Despite the fact that none of the children in the class spoke of him in a derogatory fashion, and none knew of his previous nickname ("you with a hole in your face"), he reacted to this entirely new peer group in a manner similar to his previous classmates. There he had been continuously teased and put on the defensive to protect himself both psychologically and physically.
>
> During the psychiatric evaluation the same type of behavior persisted. It was found that his provocative behavior was a means of fending off a relationship in which he felt certain he would be again rejected. This unconsciously determined behavior which did not allow others to like him helped to maintain his poor self esteem by confirming that no one cared for him. Psychiatric treatment was recommended.

Adolescence with its instability and personality reorganization poses a major hurdle for the child with a congenital defect. At this time the child becomes intensely concerned with such questions as, "Who am I? Who am I to be? What can I be? How do I behave with adults, peers, and with the opposite sex? What work will I do? Will I marry? Will I be able to have children?" These concerns coupled with the increasing awareness of one's body makes the adolescent with a congenital defect more psychologically susceptible to personality crises than the physically healthy adolescent. For example, the child with congenital atrophy of testicles becomes increasingly aware of their absence and markedly concerned about his future potentiality. The hypopituitary dwarf, whose short stature has already posed personality hurdles, is frequently unable to participate in social relationships with his peers, particularly those of the opposite sex, in other than a peripheral relationship, described by some as a "mascot." The crucial damaging blow to his self esteem is rendered when his short stature may make him unable to pass, what is commonly considered a puberty rite in the United States, the drivers license examination.

Some Considerations In Management

Parents' concerns about the normalcy of their new baby antedates its birth. It follows then, that the management of that concern plays an important role in establishing attitudes that would be most conducive to optimal care.

During the recent Rubella epidemic, many pregnant women found themselves in a dilemma. A possible exposure to Rubella, a questionable past history of having had Rubella, and the dubious effectiveness of gamma globulin were weighed against a therapeutic abortion. They had to endure eight months of uncertainty before learning whether they had guessed right or wrong; many were wrong. These women then had to mobilize their emotional resources to face the complexities of mothering a child with multiple anomalies. Some were without adequate preparation and support because their physician, relatives, and friends all too readily had joined in denying this possibility.

Similar considerations pertain to the genetically determined disorders, which, because of increasing interest in screening techniques to detect heterozygotes, may become a more frequently recognized problem. Once identified, the decision for having children with the inherent risk will still be left to the prospective parents. The role of the physician is to repeatedly provide the opportunities for the potential parents to discuss all eventualities, including a theraeutic abortion. The physican should be wary of joining them in any denial.

Some mothers who have unsuccessfully attempted self-abortion early in pregnancy find themselves overwhelmed with feelings of guilt about their deformed infant. During pregnancy they were unable to adequately resolve their ambivalent feelings, and frequently, they were even unable to tell their physician of their attempted abortion. Although the more popular "abortifacients" (manipulation, enemas, quinine, etc.) are not known to have teratological effects, the guilt feelings aroused may be a chronic problem in managing and relating to the child.

It is not unusual to hear that parents of a newborn infant with a meningomyelocele, who at birth were advised against any treatment for their "unsalvagable" child, are called two weeks later to come take the child home. The anticipated early death of the infant did not occur and now the mother and father, whose baby may never have been shown to them to spare them distress, are presented with a severe crises. Aside from the obvious complications of management resulting from an initial approach of rejection, the emotional turmoil of this child's parents can be a factor of major proportions in the development of the child and his parents. The influences of the attending physician's attitudes are of course crucial in his usefulness to the patient and family. A detailed consideration of this crucial area is beyond the scope of this discussion.

In the neonatal period, the criteria for medical intervention are generally determined by an assessment of the child's defect, the risk to life, and the technical problems involved. However, the physician must also consider the alteration of disfiguring anomalies even without necessarily improving function or saving a life if it means an improved maternal adjustment. An important goal in the early closure of cleft lips is to permit normal sucking activity necessary to both mother and child. Although rarely mentioned in favor of early closure of spina bifida sacs, the possibility of normal handling by the mother offered by that procedure may be vital to the child's nurturance.

As the child approaches the pre-school years, it usually becomes easier to evaluate psychological and physical skills. Appropriate school and habilitation programs should be based on the fullest assessment of potentialities. A periodic comprehensive inventory of both assets and liabilities guides parents, who have painstakingly tried to help their child, but who unfortunately have also developed unrealistic concepts about his capabilities. The physician may then point more realistically to the areas where their energies can be more usefully applied.

Repeated evaluations, especially of intellectual function, are necessary in order to discover factors that might be inhibiting optimal performance.

> A 6 year old girl with congenital lymphedema of one leg was withdrawn and failing scholastically. Although considered to have borderline intelligence by the school, psychological testing during her hospital admission showed her to be bright. This information led to appropriate counseling for the child, mother and teacher. After a major surgical procedure which significantly improved the appearance of her leg and the additional aid of a tutor, her school performance and peer relationships began to improve.

The young child with a visible defect invariably is confronted with a massive challenge in entering school. Adjustments to defects are made more readily in the limited home environment and immediate neighborhood, but in school abnormalities become more conspicuous. It is advantageous to provide counseling to parent, child, and teacher and to plan corrective procedures for facial, hand, and other obvious anomalies before entering school.

> A 10 year old boy with a meningomyelocele whose only major residual deficit was urinary incontinence, was brought for consultation with a complaint that his personality was extremely immature. Although physically fully ambulatory he was effectively paralyzed psychologically and socially by being completely

homebound in diapers. A schedule of bladder training gave him enough control to go to school and his entire personality began to progress in expectable developmental elaborations.

Deciding between placement in a regular or handicapped children's class is frequently a dilemma especially when intelligence is normal. The consensus of current medical and educational literature favor placing handicapped children of normal intelligence in regular classes. The emotional benefit derived from this placement not only depends on adequate teaching resources and preparation, but in a large measure on the support the child and his family receive from all sources.

As the child becomes older, the continuing process of self awareness and the recognition of his capabilities becomes more important. He must be encouraged to participate in programs in which he can succeed and thus enhance self-esteem.

Parents of newborns with congenital upper-limb amputations occasionally insist on a prosthetic limb, which is cosmetically acceptable although functionally limited. Adequately managed children frequently prefer the more functional hook device earlier and defer their interest in cosmesis until adolescence. Occasionally adolescents who have not had a prosthesis refuse to accept one. Their concept of their body image is so well entrenched that they would rather accept the handicap than change their self concept and face the prospect of a change in their functioning and an increased independence.

In adolescence vocational planning is essential. In the anticipation of future needs, a separation frequently begins which may have been delayed because the parent-child relationship had become too mutually satisfying to the dependency needs of the child and to the parents' need for a dependent. A growing sense of identity as a valuable member of society should be nurtured so that the congenitally handicapped child may some day see himself realistically as a worthwhile and independent member of the community. His limitations should not be social or emotional but those that realistically are characteristic of his physical handicap to which he can adjust by active involvement in an effective educational and medical habilitation program.

Summary

The impact of some birth defects on the development of the child have been discussed in terms of developmental, public, and parental reactions. The effect on the child's personality and consideration in management have been discussed to help those physicians attempting to prevent social and emotional handicaps in the congenitally handicapped child

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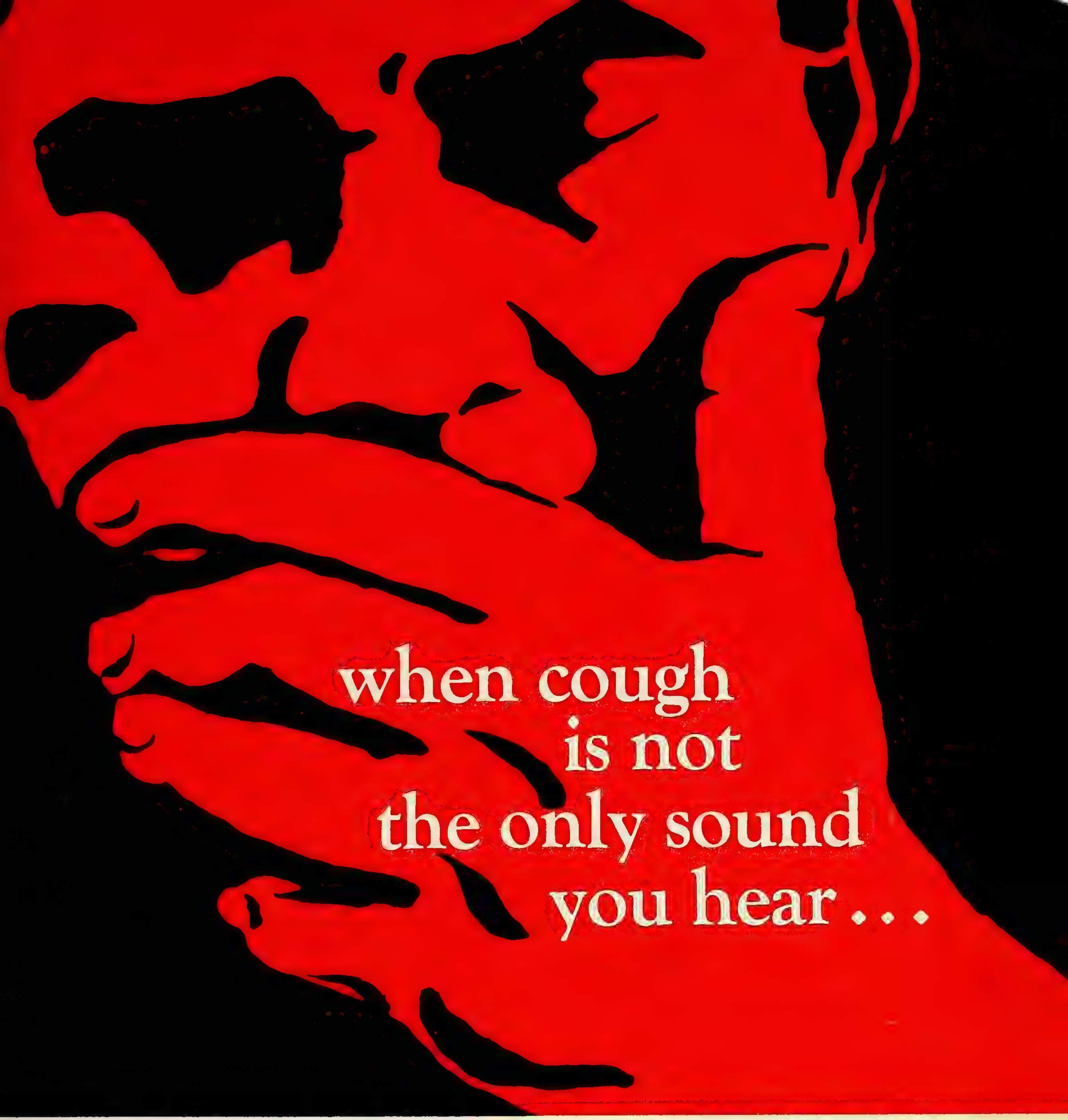

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The Impact of Maternal Deprivation on Infant Development

Martha F. Leonard, M.D.

Then his (Moses') sister said to Pharoah's daughter, "Shall I go and call you a nurse from the Hebrew women to nurse the child for you?" . . . So the girl went and called the child's mother.[1]

Adequate and inadequate parental care

The need of an infant to be mothered has been taken for granted since at least the beginning of recorded history. "Mothering" in the sense of physical care and protection of a helpless human infant is obviously essential for survival and health. Achievement of optimum physical, intellectual, and personality development requires far more than attention to physical needs. It is possible to construct a model of optimal parental care based upon clinical and research experience and knowledge which comes from living with children.

Ideally an infant has two parents, who have been loved and nurtured as children, and who have a satisfactory marital life, with mutual love, respect, and emotional support. They have matured in their respective roles of woman and wife or man and husband. Whether they have other children or not, the infant born to them is wanted. They are able to perceive him as an individual separate from themselves, with his own personality. They can understand and respond to his needs even when it interferes with their own wishes or pleasure. As they give of their love and appreciation to the infant, they receive his love and responsiveness, and grow in their roles as parents.

The mother is usually the one who assumes the close care of the infant. From her satisfying of his needs, the infant develops trust and love for her as a specific person. This relationship with her gives important incentive and meaning to his developmental advances.

The father's role is important in his supportive relationship to the mother as well as his care of the infant. His understanding of his wife's needs of special support and care during pregnancy and delivery enhances her confidence in herself as a mother. His provision for the physical needs of the family frees the mother for child care and home-making. He enjoys opportunities to take part in the baby's care and shares the responsibility for decisions about child rearing practices. He is an important model for the growing child.

Such parents can give the baby the ingredients generally accepted as essential for optimum development: loving, tender care by the same consistent people, appropriate response to needs, respect for and enjoyment of the baby as an individual, encouragement, stimulation, and at times demands for developmental advances, provision of materials for learning, such as toys and books, consistent guidance in learning acceptable behavior, opportunities for socialization and for times alone, and themselves as models for their growing children. This is not to suggest that there would not be difficulties, disagreement, and crises. These are part of life, and coping with them as a family strengthens each member for future challenges.

Although ideal parental care can probably not be attained, fortunately the resiliency and adaptability of the human child permit adequate development under a variety of less than optimal conditions. However, there are many infants—an alarming and tragic number—whose development is endangered or permanently impeded by inadequate parental care.

Maternal deprivation is here defined according to Ainsworth[2] as "insufficiency of interaction between the child and a mother figure." It includes the lack of individualized care of institutionalized children who do not have a consistent mother substitute and insufficient quality or quantity of care or interaction which some children experience when living with their own mothers or foster mothers. There may be deprivation of all areas of mothering or in just one or more aspects of maternal care.

While severe deprivation results in serious global delays in infant development, specific types of qualitative and quantitative maternal deprivation affect specific areas of the infant's general develop-

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ment and learning. Lack of adequate stimulation and encouragement for motor development may cause significant delays in the appearance of gross motor landmarks with relatively good development in other areas. On the other hand, over-stimulation in motor activities and bodily contact with lack of encouragement for use of toys may delay a child's ability to work out solutions for himself and lead to hyperactivity and poor impulse control. Lack of encouragement or opportunity for verbal interchange may significantly delay speech development and use of language for learning and reasoning tasks. This has been illustrated by studies of culturally deprived children. The infant who is cared for by a number of different people may receive adequate physical care and stimulation, but is deprived of a special close relationship with one need-satisfying person. This closeness is necessary to establish the personal bond on which sturdy development is based. When these close bonds with one or two persons are lacking, it is likely to affect personality development, causing indiscriminateness in relationships and difficulty in forming close friendships. In all instances, the effect of deviations in parental care on the development of the infant depend on both the innate characteristics of the infant and the nature, duration, and timing of the deprivation.

Case Reports

Our research studies of infants with "failure to thrive" in the Pediatric Department of the Yale New Haven Hospital have included developmental evaluations of each infant. Many of these infants have had developmental delays which have been correlated with varying kinds and degrees of maternal deprivation or difficulties in mother-child relationship. Vignettes from the histories of two of these infants serve to compare the developmental and nutritional changes in a severely deprived infant with those in a baby whose deprivation was in specific areas.

Case No. 1 Linda B. was the second child of 23 year old parents and was 1 year old when she was admitted to the hospital for failure to thrive. Mrs. B's poor nutrition and her parents' disinterest were of concern when she was seen in the Pediatric Out-Patient Department during her own childhood. She left home at 15 because of her step-father's criticisms and sexual advances and delivered her first child out of wedlock at 20. She married shortly before Linda's birth, but her husband was not supportive, and much marital difficulty ensued. Soon after Linda's birth Mrs. B. was found to have active pulmonary tuberculosis. With inadequate treatment, she went back to work, leaving Linda in the care of baby sitters. At the time of Linda's admission, the mother was six months pregnant, with no arrangement for prenatal care.

Mrs. B. was ill prepared for the major crises of illness, financial insecurity, troubled marriage, demands of two babies, and pregnancy. She was an attactive young woman, but disorganization was apparent in her careless dress, deplorable housekeeping, and difficulty in thinking clearly about the reality of her situation. She was preoccupied by her problems, discouraged, fearful of her husband, and angry. She was manipulative and distorting in her efforts to obtain material things for herself and the children, but defensive and unable to accept guidance. She had an infantile personality and a tendency to blame others for her difficulties. She seemed unaware of the needs of her children or her role in their poor growth. The children were probably left alone at times, and even their physical needs were poorly met. Their mother rarely cuddled, played, or talked with them.

Mr. B. was never seen, since he was in jail, but Mrs. B. reported that he was unpredictable, difficult, and had a quick temper.

Although she was born at term, Linda weighted only 2.4 Kg. (5¼ lb.) and was 46 cm. (18 in.) long. On her several emergency room visits for rashes, abrasions, and respiratory infection, she was described as "scawny," but eating well. At 6 months the visiting nurse noted that Linda looked retarded, but the nurses's contacts were discontinued because of Mr. B's objection, and appointments to clinic were not kept. When Linda was brought to the emergency room at 1 year because of aspiration and difficulty in breathing, she was a markedly underdeveloped and marasmic baby, looking and acting more like a 4 month old infant. She weighed 6.0 Kg. (13 lb. 3 oz.) and was 67 cm (26½ in.) tall. Head circumference was 41 cm. (50th per centile for a 3 month old girl.) She was inactive and irritable, and her main spontaneous activity was to pull a sheet over her face. Pustules and peeling skin in the diaper area were the only physical abnormalities besides her emaciation. Bone age by roentgenogram was estimated as 3-6 months. Other laboratory tests were within normal limits except for mild anemia.

Linda showed marked delay in all areas of development and considerable unevenness (See Table 1). The most severe lag was in gross motor development. She was a very quiet baby, who lay very still, and her movements had little strength or vigor. She had minimal postural tone and was unable to move around in the crib, except for rare rolling—a recent accomplishment. In contrast to her severely delayed gross motor skills, she showed fairly good grasping patterns of large and small objects. She had little interest in toys at first, but with coaxing she began to use them with a little pleasure. She could reach, grasp and transfer from hand to hand. She did not explore other possibilities of using the toys, even of mouthing them. She did not try to retrieve a lost toy. She responded to sound, but did not show understanding of any words, and was not heard to make any meaningful words. She showed no anxiety toward strangers but was watchful of everyone. Smiles were hard to coax but were elicited with a game of peek-a-boo. She made no response to offers of picking her up, but when held, clung tightly with legs flexed.

Linda's development was delayed in all sectors. The unevenness and the relative superiority of her fine motor and adaptive skills to gross motor and language development suggested that Linda had a potential for better de-

Table I. Developmental Characteristics

	GROSS MOTOR	FINE MOTOR	ADAPTIVE	LANGUAGE	PERSONAL-SOCIAL
Linda B., age 1 year	16-24 week level Quiet, inactive Poor control of head and back—no sitting Rare rolling Little weight on feet	40 week level Fairly good dexterity in grasping large and small objects	33-44 week level Very uneven Grasps, holds, transfers, removes No combining No exploration No memory for object hidden under diaper	28-40 week level Quiet Response to name, no other comprehension Reported to say dada, mama, but not observed	Quiet, apathetic or irritable Very watchful No sranger anxiety Not cuddly—stiff No mouthing or play with feet No anticipation of being picked up. Prefers to lie with diaper over face
Jimmy K., age 27 weeks	20-24 week level Quiet, inactive no effort to change position Assists on pull-to-sit Sits slumped Supports weight on feet	24-28 week level Good reach and grasp	28 week level Only visual interest at first Grasps, holds, shakes bangs, mouths Looks vaguely for hidden toy	24 week level Quiet at first increasing responsive coos and grunts	Very placid, lies for hours sucking thumb Plays with feet No sustained interest in people No stranger anxiety Not cuddly—stiff No anticipatory activity

velopment, but that her progress had been impeded by massive deprivation of maternal interest and stimulation.

During three weeks in the hospital, Linda gained 1½ pounds, became cheerful and animated, learned to sit alone, and to play some simple hand games. She made many more sounds, and became more demanding of adult attention. This acceleration in development substantiated the prediction of her potential for better learning. However, it was not possible to find an effective way to help the mother. She had many excuses for not visiting Linda, and her worry about her husband and her pregnancy took precedence over consideration of ways in which she could enjoy Linda's new achievements and promote further development. In spite of coordinated plans for continued support to Mrs. B. by the public health nurse, and both welfare and hospital social workers, Mrs. B. denied the need of help and refused it. She delivered a healthy baby girl, who was admitted to the hospital at the age of 3½ months for severe failure to thrive. The family was found to be living in a state of filth and disorganization. Linda was still small at 18 months, a very sober, sad little girl, who had no speech.

Linda was massively deprived in all areas. She probably received inadequate food, and her diaper rash attested to her lack of physical care. She had not been held or cuddled much and had not learned to anticipate pleasant and predictable activities. Hence, she was soberly watchful or shut out the environment with her sheet. Lack of interest of others in her was reflected in her lack of interest in her own body, for she did not put things into her mouth or play with her feet. Inadequate stimulation and insufficient food for energy gave her no incentive for development of gross motor skills or play with toys. Minimal exposure to language was reflected in minimal vocal output. Her fine motor development, which is less vulnerable than gross motor development to environmental influences, was relatively good although not age adequate. This and her ability to use toys after considerable play and coaxing, suggested that her potential for learning was better than her initial performance, and that she might develop more adequately if her environment could be improved.

Case No. 2 Jimmy K. was first seen at the age of six months because of spitting up and failure to gain weight. He was the seventh child of 41 year old parents. Jimmy's mother was a college graduate who had experienced a mild postpartum depression with each pregnancy, and had been more severely depressed after Jimmy's birth. His father was a foreman who participated actively in the family life. Both parents were quiet, easy-going, compliant, and mutually supportive. The other children were aged 3 to 19 years, and the oldest helped with the care of the young children. This was a stable family, with many strengths, and the parents were able to make good use of professional help when needed. There were affectionate and helpful contacts with members of the extended family.

Jimmy weighed 3.8 Kg. (8 lb. 5 oz.) at birth, and had an uneventful neonatal period. At about 6 weeks he began to vomit and soon progressed to projectile vomiting in spite of at least eight formula changes. He gained well to 4 months and then very slowly. He had frequent, poorly understood febrile illnesses. His pediatrician was concerned that he might be a little retarded because of his slumped sitting position and lack of reaching for toys. He was an attractive, but thin, frail, and sickly-appearing baby, with large blue eyes, pale skin, and very little activity or interest in anything but sucking his thumb. He was 64¼ cm. (25¼ in.) long, weighed 6.4 Kg. (14 lb.) and had a head circumference of 43 cm. (17 in.) No physical cause was found for his poor weight gain. He often lay in tonic neck reflex position. His hands were closed, but not tightly fisted.

When Jimmy was first evaluated at 27 weeks, he was functioning in the average range except for a little delay in gross motor skills and in socialization. (See Table 1) He had very little motor drive and made no effort to move toward a desired object just beyond his reach. He slumped in sitting position, although he could bear most of his weight when supported on his feet. In supine he lifted his legs high and played with his feet. Although he had only visual interest in toys at first, with much encouragement he began to handle them and to become increasingly animated and excited. He was able to hold two at once, shake, bang, mouth, and transfer. He hung on to toys he liked, but made no protest when they were taken away. He was quiet at first, but vocalized increasingly in a variety of responsive coo asnd grunts. He was a very placid baby, with no apparent stranger anxiety. He made no effort to initiate contacts with another person, did not show sustained interest, or anticipate familiar behavior. Sucking his thumb seemed to give him the greatest satisfaction.

The evaluation showed that he was not mentally defective. His minimal motor drive, delay in gross motor skills, and limited interest in people or things were compatible with deprivation in the areas of suboptimal stimulation for motor activity, socialization, and use of toys.

Because of minimal weight gain and little progress in motor development, he was admitted to the Children's Research Unit at 9½ months, and his mother roomed in with him. It was feared by some of the hospital staff that he might have brain disease. He could not sit well, creep, or pull to stand, and said no specific words. Observations of mother and baby together were significant. Mrs. K. was loving, gentle, and competent, but subdued and quiet. She sat near her baby, looked at him and smiled, or wheeled him in a stroller, but rarely held him, talked to him or played with him.

With the daily active encouragement of nurses and pediatricians and the increasingly active participation of the mother, Jimmy's progress was exciting to everyone, especially to him. Every day saw a new advance. With one brief demonstration he learned to pull to stand, and was soon walking with support. He became increasingly interested in toys and people, and much more vocal. His color improved, and be began to look healthy. Mrs. K. gratefully benefited by the support of the staff, and was thrilled by Jimmy's progress, gaining confidence in his health and good prognosis, and her role in maintaining it. The mother and the whole family continued active play with Jimmy after discharge. He walked alone at 15 months and by 18 months was talking in many single words. His weight gain paralleled his developmental spurt. When recently seen, at the age of 28 months, his height and weight were in the 50-75th percentile and his development was age adequate in all sectors. He was a robust and vigorous little boy, happy, curious, independent, talking freely in sentences.

The mother's depressed mood with its impact on her style of child care was the major factor in his symptomatology. She preferred to keep Jimmy quiet in crib or carriage, and this mode of care was further suggested by his fragile appearance and tendency to vomit. Jimmy's placid disposition contributed to his understimulation, since he rarely demanded attention. He received adequate food and considerable affection and appreciation from his family. However, he was rarely held or exercised, and toys had not been made interesting to him. He enjoyed playing with his own body, but had little interest in toys or people.

These two infants illustrate some of the effects of deprivation of optimum nurturing upon development. The common features in the two infants were impaired physical growth, delayed gross motor development, minimal interest in toys, and certain deviations in social interaction. The child with more severe deprivation had more serious impairment, which involved all sectors of her development. Both infants were first thought to be retarded and one to have a possible neurologic deficit because of delayed motor development. Results of the developmental assessment of both infants suggested that the lags were at least in part environmentally induced. Knowledge of each infant's family and home life, aided by a period of hospitalization and observation of mother and infant together supported this formulation. Further proof came from demonstration of improvement in the developmental pattern by alteration in the infant's care.

Brief Historical Review

Early research on the effects of withholding from infants a natural relationship with a mother, conducted at the command of Frederick II, German King and Emperor of the Holy Roman Empire in the thirteenth century, showed dire effects.[3] All the infants died. Many events have corroborated the tragic consequences of totally inadequate infant care.

The institutionalized child has been the focus of many types of observation, which have documented the deleterious effects of maternal deprivation. Bowlby[4] and Ainsworth[2] have summarized the work of many investigators of this subject. Bowlby concluded that lack of adequate maternal care for children in institutions was a major cause of adverse development. Provence and Lipton made detailed developmental studies of infants in an understaffed orphanage compared with others reared in their own homes.[5] Their data demonstrate dramatically the progressive deceleration and deviation of development in the institutionalized infants from the third month of life, leading to function in the retarded range by the age of one year. Study of these severely deprived infants and their characteristic developmental profiles led Drs. Provence and Lipton to the recognition of similar milder alterations in development in infants in their own homes.[6] Adverse changes in the developmental patterns of several healthy babies were concomitant with problems in the mother or in the relationship between mother and baby, which seriously interfered with each mother's ability to nurture her infant. This demonstrated that care of an infant by his own mother could include some inadequate or disadvantageous features which were reflected in slowing or altering the infant's development. When the mother's ability to nurture her infant could be strengthened, developmental advances could be seen in the infant.

Yarrow has delineated some of the differences in impact of maternal deprivation depending on its timing in the infant's life, duration, permanency, and opportunity for a previous establishment of a strong mother-child relationship.[7]

Deprivation of adequate maternal care and stimulation may also cause delays in physical growth and weight gain. Many studies have described this relationship, including Widdowson's observations in two post-war German orphanages,[8] and the growing literature on infants and children with failure to thrive.[9-12] Some of the most severe growth retardation has accompanied the seriously adverse parent-child relationship leading to child abuse. Powell, Brasel, and Blizzard have shown that a number of abused children with markedly delayed growth had a decrease in pituitary growth hormone, which returned to normal quickly when the environment was improved; later they accelerated in growth.[13]

Discussion

While biologic maturation proceeds in an orderly sequence in normally endowed children, the use to which emerging structures and functions are put depends on the life experiences of the developing infant and his relationship to significant adults. Functions which are not repeated and exercised may be undeveloped or deviant. Most of the climate of the early months is determined by the mother-child relationship. Many kinds of stimuli and experiences are included in "good maternal care": the mother's continuing closeness, fondling, tenderness in physical care, introduction of toys, vocal interchange, and appreciation of advances encourage and stimulate the baby to develop. His development and increasing skills and his pleasure in enjoying them with her, further enhance the mother's own development as a woman, with capacity for mothering.

If the baby is massively deprived of most aspects of nurturing care, there is a global interference with his development, and he may also be delayed in growth and weight gain. Tasks for which the body and central nervous system have matured adequately are not attempted or perfected. (For example, Linda did not sit alone at one year, although she learned how after a few days of encouragement.) If neither the mother nor anyone else has provided and supported the child's play with toys he will have little incentive to learn how to use them. If his vocalizations are not responded to and he hears little language, he does not develop much speech. If he is not handled, he loses one of the important sources of contact and also may not learn to know his own body. (Linda's absence of sucking or play with her feet.)

However, deprivation is often not total, but may involve one or more aspects of maternal care, and may be permanent, temporary or recurrent. According to Provence and Lipton "The effects of maternal deprivation on an infant in the first year of life depend upon the degree of deficit in both the quantity and quality of maternal care, upon the infant's biological endowment, and upon the age and length of time he is subjected to the deprivation. Many individual combinations of these factors are possible, and produce a variety of clinical pictures in terms of severity of symptoms."[5]

Deprivation is not equated with rejection, hostility, or deliberate neglect. Although it usually accompanies these severe deviations in a mother's attitude toward her child, it may also occur to an infant whose mother loves him dearly. A mother who is overwhelmed by financial burdens, frequent pregnancies, illness, immaturity, or personality disorder may be unable to give of herself to her infant in a nurturing, supportive way. A mother who has never experienced a nurturing kind of mothering herself has no adequate model for motherhood. Maternal depression especially interferes with energy or incentive to cuddle a baby, play with him, talk with him, or encourage the development of his emerging skills.

Deprivation in certain areas of maternal care may result in specific developmental lags in spite of satisfactory mothering in other ways. Jimmy's history illustrates a common deviation—delay in gross motor development when a child experiences little handling or stimulation for motor activity. Delays in language development are also common if the mother is depressed, preoccupied, or taciturn. The specific areas of impact on development depend on the style of mothering, the degree to which it deviates from optimal stimulation, the length of time the baby is understimulated, and his stage of development when this occurs. The extent of the impact on the child obviously depends also on the nature of the child. A demanding baby would have required more handling than Jimmy; or one with a strong motor drive might have made more motor progress without much encouragement. His placid, quiet nature allowed him to suck his thumb peacefully and just watch the activity around him. Yet after he was urged and encouraged to become active, he derived especial pleasure from his motor pursuits.

When a baby's development is believed to be delayed by maternal deprivation, assistance can be offered to both mother and baby. The mother can receive sympathetic interest from the physician and concern for her as a person and for her needs. If possible she can be directed toward tangible help for any overwhelming problems, such as financial assistance, medical care, marital counseling or family planning. The mother can also be reassured about the baby's assets and potential and shown ways of doing things with him which will stimulate further development. If the baby is hospitalized for evaluation of growth and developmental delays, it is important to encourage participation of the parents in the diagnostic and therapeutic plan. This provides direct observations of the way the mother and father deal with the child, and opportunities for the staff to give encouragement to the mother, to demonstrate ways of promoting a child's development, and to involve her in such activities so that she will be associated actively with the baby's improvement. A public health nurse, homemaker, or health aide can give assistance and encouragement to the mother at home. Others can assist in carrying out active efforts to promote the baby's development—the father, older siblings, other relatives, or friends. As the mother participates in activities with her child she will gain confidence in herself as a mother and respond with pleasure to her baby's advances. His awareness of her pleasure increases his incentive for more progress. After a baby has started to become more active, he may elicit more interest and involvement from his parents.

The outlook is good for reversibility of developmental delays caused by deprivation or understimulation when they have not existed too long and when the baby's care can be changed. The experience of Provence and Lipton[5] and others indicates that severe deprivation over a prolonged period may lead to permanent retardation or deleterious effects on intellectual performance, character and personality development in spite of adequate endowment for learning.

Prevention of developmental deviations is far preferable to attempts at amelioration. Physicians, public health nurses, and social workers serving families with young children have the opportunity to recognize high risk families, and to begin supportive measures in prenatal clinics or child health conferences. Mothers can be helped to watch for the child's developmental progress, and anticipatory guidance can include both suggestions and examples of ways to hold, play with, and talk to a baby to promote his development. Slowing of development or failure to gain and grow adequately are signs of trouble and indications for definitive pediatric and developmental evaluation and exploration of the family setting.

Conclusions

Two case reports are cited to illustrate effects of generalized and partial deprivation of maternal care and stimulation on the growth and development of young infants. Similarities and differences in their developmental profiles are outlined. Developmental delay is one symptom of maternal deprivation, and an indication for careful assessment of child and family, and for early intervention. Attention to the needs of the parents and the infant is important for effective and sustained improvement. Reversibility of developmental delays is demonstrated.

This research was supported by the Connecticut State Department of Health; the Children's Bureau and National Institutes of Health, U.S. Department of Health, Education, and Welfare; and the Grant Foundation.

The patients reported were studied in the Yale Pediatric Clinical Research Center, supported by U.S. Public Health Service grant No. FR00125-02.

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Resolution Regarding Poliomyelitis Adopted By The Conference Of State And Territorial Epidemiologists

March 13, 1968

WHEREAS, as a result of the marked reduction in incidence of poliomyelitis, the index of suspicion has waned and the urgency for prompt reporting has apparently diminished thus permitting the evolution of minimal localized outbreaks with subsequent delay in control procedures and because the pressure to maintain immunization levels may be diminished.

NOW THEREFORE BE IT RESOLVED that state and territorial epidemiologists immediately re-emphasize to the medical profession and to health departments the need for continuing aggressive surveillance of poliomyelitis, including prompt reporting of suspicious and diagnosed case, epidemiological investigation of circumstances of infection, early submission of appropriate laboratory specimens, institution of epidemic control procedures and renewal of effective immunization programs for preschool children.

FROM THE GENERAL MANAGER'S OFFICE

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Director of Public Relations

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SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, April 18, 1968

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin were: Drs. Bradley, Grendon, Polivy, Brandon, Caplan, Fabro, Hess, Rogol, Cramer, Egan, Abbot, Shepard, Johnson, Grant, Petrie, Pelz, Roch and Granoff.

Also present were: Mrs. Lindquist, Mr. Villano and Dr. Richards.

Absent were: Drs. Gardner, Spitz, Hastings, Ayres, Nolan, Jacobson, Jr., Wilson and Palomba.

II. ROUTINE BUSINESS

Date of Next Meeting

In accordance with the Bylaws, the President will call the organizational meeting of the Council for 1968-69 "as soon as possible" following the Annual Meeting of the Society, April 30-May 2, 1968.

III. OLD, NEW AND SPECIAL BUSINESS

Announcement—Formation of Genetics Information Center

Submitted by Stewart P. Seigle, Hartford, an announcement that a new Genetics Information Center has been established by the State Health Department was accepted as information, and with thanks. The Center is intended to serve two purposes: (a) To answer questions for physicians who run into genetics problems, and (b) To identify those physicians in the State who have an interest in, and/or knowledge of, genetics.

Reports—Council's Fiscal Advisory Committee

Actions were taken on three reports of the FAC as follows:

(a) It was VOTED to approve the FAC's recommendation that 1968 membership dues in the amount of $30.00 be paid to the New Haven Taxpayers Research Council, Inc.

(b) It was VOTED to approve the FAC's recommendation that, at this time, the Society *not* make a contribution to The Connecticut Society for the Prevention of Cruelty to People, Inc.

(c) Since substantial outside funds have been obtained to cover some of the costs of a "Physicians Workshop on Sex Education" (arranged by the Public Relations Division and the Committee on Public Health), it was VOTED to approve the recommendation of the FAC that the previous (3/6/68) allocation of CSMS funds for this purpose be reduced from "up to $1500" to "up to $500."

Nomination to the Governor—Board of Examiners for Hypertrichologists

From a list of several qualified dermatologists, it was VOTED to nominate to Governor Dempsey for appointment to the BEH as a replacement for Ellwood C. Weise, Sr., Bridgeport, (resigned) Ralph L. Parker, Bridgeport. The current three-year term (given up by Dr. Weise) will expire on June 30, 1969.

Reports—Committee on Public Health

After making several amendments, it was VOTED to adopt, as amended, a resolution submitted by the Committee on Public Health which reads as follows:

WHEREAS: There is evidence in the number of cases of venereal disease, illegitimacy, early teen-age marriages, divorces, broken homes, and related problems, of the inability of many people to cope with the facts of family life and sexuality; and

WHEREAS: Health education and the dissemination of factual health information are necessary to the development of an individual's ability for critical decision making; and

WHEREAS: Youth has a right and a need to have such information on matters of interest and/or concern to them; therefore be it

RESOLVED: That the Connecticut State Medical Society encourage appropriate efforts to develop and strengthen family life and sex education in the community, and, particularly, in the schools; and be it further

RESOLVED: That the Connecticut State Medical Society urge the individual physician to assume his responsibility for family life and sex education for his own patients, in the community, and as a medical advisor to schools.

Report—Ad Hoc Committee to Study Problems of Abortion

It was VOTED to approve, as amended by the Council, a report of this Ad Hoc Committee which presented a "Statement of Policy re Therapeutic Abortion" based on much the same principles as that adopted by the AMA House of Delegates in June of 1967. It was further VOTED to transmit this statement, as amended, to the House of Delegates with the recommendation of the Council that it be adopted. A copy of the report of Reference Committee G, AMA House of Delegates, Atlantic City, June 18-22, 1967, will accompany the statement as background information. It was further VOTED *not* to accompany the statement with the full report of the AMA Committee on Human Reproduction as suggested by the Ad HOC Committee, but to publish the AMA Committee's subject report in an early issue of the Journal.

Request—Connecticut Regional Medical Program

It was VOTED to defer action, for the present, on a request from CRMP that the Council nominate a member of the Society to serve with a "technical advisory committee" to CRMP's developing "Program for the Routine Assembly of Patient Care Information." Following rather lengthy discussion of this and other matters relating to the structure and goals of the Connecticut Regional Medical Program, it was VOTED to transmit to the forthcoming meeting of the CSMS House of Delegates a resolution as follows:

SUBJECT: REVIEW AND REEVALUATION OF REGIONAL MEDICAL PROGRAM

WHEREAS: The Connecticut State Medical Society has a proper and sincere concern that the Connecticut Regional Medical Program will be successful; therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society direct the Council to request of the Connecticut Regional Medical Program a review and reevaluation of the latter's goals and structure.

Request for Nominations—Advisory Committee on Child Abuse

Having been apprised that the State Commissioner of Health is establishing an Advisory Committee on Child Abuse, and of his request that the Society nominate two members of the CSMS Committee on Public Health to serve with the new Advisory Committee, the Council VOTED to submit nominations to the Commissioner as follows:

Clarence W. Harwood, Middletown
Edward T. Wakeman, New Haven
Joseph J. Bellizzi Hartford

Placement Opportunities

INTERNIST urgently needed for community near Hartford, Connecticut. Rapidly expanding General Hospital serving a population of 30,000 needs internist to head the Department of Medicine and establish a private practice. Outstanding opportunity will be partially subsidized by the hospital and will be welcomed by a friendly Medical Staff.

WANTED: Young pediatrician to join two internists and two general practitioners in a new medical building complete with laboratory and radiology services in a beatiful suburb of Hartford, Connecticut. Type of arrangement offered flexible.

NEEDED: PEDIATRICIAN—For area of 60,000 in Northwestern Connecticut which has lost two of its three pediatricians to retirement and clinical research. Ample office space in principal area city. Progressive local hospital has full range of specialty services. For further information, write or call: John Nicklas, Executive Director, The Charlotte Hungerford Hospital, Torrington, Connecticut 06790.

DERMATOLOGIST—Board certified or eligible to take over a well established practice in central Connecticut, virtually unopposed, in growing area of 100,000, excellent income. Will introduce.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

SUMMARY OF PROCEEDINGS
HOUSE OF DELEGATES — ANNUAL MEETING
Hartford, Connecticut — April 30-May 1, 1968

Reports And Addresses

The House received reports and/or addresses from the President, the Secretary, the Treasurer, the Chairman of the Council, the President of the Woman's Auxiliary to CSMS, and the Chairman of the Board of Directors of COMPAC. The membership report of the Secretary and the address of the President appear at the end of this summary.

Elections

A full slate of officers, committees, representatives and advisors was elected for the terms prescribed in the bylaws.

The officers elected are:

President: Norman H. Gardner, East Hampton
President-Elect: Stevens J. Martin, Hartford
Vice-President: Max Caplan, Meriden
Secretary: Frederick C. Weber, Jr., Greenwich
Treasurer: David A. Grendon, Sharon
Speaker of the House: Kenneth F. Brandon, Hartford
Vice-Speaker of the House: Frank K. Abbot, Waterbury
Councilor-at-Large: E. Tremain Bradley, Norwalk

AMA Delegates (January 1, 1969 to December 31, 1970:

Delegate: Max Caplan, Meriden
Alternate Delegate: Sidney L. Cramer, Hartford
Delegate: J. Alfred Fabro, Torrington
Alternate Delegate: E. Tremain Bradley, Norwalk

All those elected will be formally notified by letter of their election, and their names and assignments will be published in the August 1968 Roster.

Presentations And Awards

1968 CSMS Press Awards:

Press awards, consisting of an engraved bronze plaque and a check in the amount of $150, were presented to the following:

Marjorie Harthan, *The Hartford Times*—Medical News Reporting

Ned Thomas, *The New Haven Register*—Medical Feature Writing

E. Malcolm Stannard; John Cleary; Sereno Gammell, *The Hartford Times*—Medical Editorials

Certificates of Commendation:

Certificates of commendation were presented to representatives of seven outdoor advertising agencies which participated in the Society's health careers recruiting drive. The agencies donated a total of 76 billboards to the project.

The recipients were:

United Advertising Corporation, New Haven
Bolte Advertising Company, Hartford
Murphy Advertising Company, Waterbury
John Donnelly and Sons, Norwich
Murphy, Inc., Bridgeport
Frey Advertising Company, Torrington
Standish-Johnson Company, Providence, R.I.

AMA-ERF Grants:

Furnished by the American Medical Association's Education and Research Foundation, unrestricted grants were made as follows:

To the Yale University School of Medicine—$4,875.60

To the University of Connecticut Medical School—$2,061.40

Since 1951, AMA-ERF has distributed approximately $20 million to more than 85 approved medical schools. The fund is supported by contributions from physicians and their families.

Presentation of Past President's Pin:

In appreciation of his many contributions to the Society and its members, E. Tremain Bradley, Norwalk, received a Past President's Pin as he retired from office (1967-68). Making the presentation was Stevens J. Martin, Hartford, Chairman of the Council and President-Elect. Relating to this award, the House voted to accept Dr. Bradley's presidential address with commendation and to take cognizance of "his outstanding service and his efforts on behalf of the profession."

Adoption Of Resolutions

The following resolutions were adopted by the House:

Resolution No. 2 (Introduced by the Council)

Subject: Review and Reevaluation of Regional Medical Program

RESOLVED: That the House of Delegates of the Connecticut State Medical Society direct the Council to request of the Connecticut Regional Medical Program a review and reevaluation of the latter's goals and structure.

Resolution No. 3 (Introduced by the Fairfield County Medical Association):

Subject: Physician Representation in Comprehensive Health Planning

RESOLVED: That the House of Delegates of the Connecticut State Medical Society urge the Governor's Advisory Council to the P.L. 89-749 program to communicate with the Connecticut State Medical Society with regard to assuring adequate and effective representation of practicing physicians in comprehensive health planning.

CSMS Policy Statement On Therapeutic Abortion

After making several minor amendments to a report introduced by the Council, which had been prepared by the Council's Ad Hoc Committee to Study the Problems of Abortion, the House voted to adopt a policy statement on therapeutic abortion which places the Society on record as recommending "the revision of the Connecticut Statutes so as to permit the performance of therapeutic abortion" when stringent conditions stipulated in the statement are met, and which makes it "consistent with the principles of ethics of the Connecticut State Medical Society for (member) physicians to provide medical information to the Connecticut General Assembly in its consideration of revision and/or the development of new legislation regarding therapeutic abortion." The statement also recognizes "that there are many physicians who, on moral or religious grounds, oppose therapeutic abortion under any circumstances."

The adopted statement and pertinent background material brought to the attention of the House is published in this issue of the Journal.

Evaluation Of New Format

This meeting of the House of Delegates was extended over a two-day period, with the "opening" session being held in the forenoon of Tuesday, April 30, and the "final" session in the afternoon of Wednesday, May 1. Between these sessions (Tuesday afternoon) four Reference Committee hearings were held. Through the courtesy of Lee Isenberg Associates, printed copies of the Reference Committee reports were made available to the Delegates prior to convening of the final session. In the course of discussion of a motion from the floor which would have limited future meetings of the House to one day, there were many expressions of opinion that the new format had proven to be of great value and should be continued. It was evident that the vast majority of Delegates favored such continuance, since the motion to revert to the old format was defeated by an overwhelming majority.

Establishment Of A "Judicial Committee"

Held over for action from the semi-annual meeting of the House of Delegates last December, it was voted to adopt a series of amendments to the CSMS Bylaws which establishes a "Judicial Committee" as the Board of Censors of the Society (formerly a function of the Council) and grants considerable latitude of action to the Judicial Committee in a variety of matters pertaining to medical ethics and professional deportment.

Commendation Of Journal Editor

In adopting a section of the report of Reference Committee "B," the House voted to recognize officially that "Dr. Louis H. Nahum, New Haven, has demonstrated remarkable leadership as Editor of *Connecticut Medicine*," and to give approval to Dr. Nahum's guiding philosophy in publishing a medical journal; i.e., that "our task is to help our readers in the pursuit of their profession. This requires attention to three main tasks: to record what is new, to educate and to provide a forum for discussion. Obviously, this requires that we have in mind all aspects of medicine, including medico-political affairs."

Other Actions

After careful study by the several Reference Committees, all reports received from officers, Divisional Boards, the Council and other sources were adopted. Actions on pertinent recommendations contained in these reports are recorded above.

Membership Report Of The Secretary

FAIRFIELD COUNTY			
Membership—January 1. 1967			954
New Members		44	
Less (Deaths	10		
(Resignations	2		
(Transfers	6		
(Non-payment dues	2		
	20		
NET GAIN			24
Membership—December 31, 1967			978
HARTFORD COUNTY			
Membership—January 1, 1967			1120
New Members		39	

Less (Deaths	12		
(Resignations	8		
(Transfers	2		
(Non-payment dues	9		
	31		
NET GAIN			8
Membership—December 31, 1967			1128

LITCHFIELD COUNTY

Membership—January 1, 1967			150
New Members		9	
Less (Deaths	4		
(Resignations	2		
(Transfers	2		
(Non-payment dues	4		
	12		
NET LOSS			3
Membership—December 31, 1967			147

MIDDLESEX COUNTY

Membership—January 1, 1967			118
New Members		9	
Less (Deaths	3		
(Resignations	2		
(Transfers	2		
(Non-payment dues	2		
	9		
NET GAIN			0
Membership—December 31, 1967			118

NEW HAVEN COUNTY

Membership—January 1, 1967			1020
New Members		51	
Less (Deaths	12		
(Resignations	20		
(Transfers	3		
(Non-payment dues	7		
	42		
NET GAIN			9
Membership—December 31, 1967			1029

NEW LONDON COUNTY

Membership—January 1, 1967			206
New Members		11	
Less (Deaths	2		
(Resignations	1		
(Transfers	0		
(Non-payment dues	2		
	5		
NET GAIN			6
Membership—December 31, 1967			212

TOLLAND COUNTY

Membership—January 1, 1967			29
New Members		2	
Less (Deaths	0		
(Resignations	1		
(Transfers	1		
(Non-payment dues	0		
	2		
NET GAIN			0
Membership—December 31, 1967			29

WINDHAM COUNTY

Membership—January 1, 18967			74
New Members		2	
Less (Deaths	1		
(Resignations	0		
(Transfers	0		
(Non-payment dues	1		
	2		
NET GAIN			0
Membership—December 31, 1967			74

ASSOCIATE MEMBERS	10	
New Members	0	
Less Deaths	1	
	9	December 31, 1967

Total Society Membership—January 1, 1967			3671
New Members			167
			3838
Less (Deaths	44		
(Resignations	36		
(Transfers	16		
(Non-payment dues	27		123
Total Society Membership—December 31, 1967			3715
NET GAIN FOR YEAR		44	

TOTALS

FAIRFIELD	978
HARTFORD	1128
LITCHFIELD	147
MIDDLESEX	118
NEW HAVEN	1029
NEW LONDON	212
TOLLAND	29
WINDHAM	74
	3715
ASSOCIATE MEMBERS	9

ADDRESS OF THE PRESIDENT

E. Tremain Bradley, Norwalk

Mr. Speaker, members of the House, welcome guests:

The imminent end of my term as your President stirs up various emotions, four in particular.

I. Relief: The weight of responsibility has somewhat depressed the shoulders—though not the spirit.

II. Appreciation: We are all grateful to Drs. Eckhart and Babbott, who, with their Committee, have enlisted an outstanding group of speakers on topics of importance and interest to us all, and dove-tailed the program beautifully into the three-day format. Essential to accomplishing the work of the year, as well as making it pleasant, was the stalwart support of the General Manager, Dr. Richards, his delightful-to-work-with assistant, Mrs. Josephine Lindquist, and her most helpful staff, and our dynamic and effective Public Relations Director, Mr. Peter Villano. The members of the Council and various committee chairmen have shown great cooperation and much tolerance when my sense of urgency was aggravated by the running-on of the calendar and by pressure of public trends. Thanks also go to the colleagues who gave me confidence that my patients were well cared for while I attended to the affairs of the Society. The Woman's Auxiliary, under the able leadership of Mrs. Anthony Cipriano, has again performed an outstanding service. To honor the start of their twenty-fifth year, dancing has been added to the Annual Dinner tomorrow night where we expect to see as many members and their wives as possible. My own woman's auxiliary, my office staff, has cheerfully made infinite readjustments and performed many functions strictly for the Society. At this time, let me pay tribute to Mr. Arnold Olson, whose sage judgment and stabilizing influence over the past ten years have given me courage to take on successive assignments. His contribution has been great to the Fairfield County Medical Association, where he is Executive Secretary, but in his quiet, impartial, very modest way, he has done a lot, too, for the Society. About my wife, Marilyn, who had the courage to marry me last June, who expects to graduate from Vassar next month, and who has lifted me up in so many ways, little need be said. I'm sure it shows.

III. Gratification: Much has been accomplished during the year, old brass polished and new endeavors undertaken. The fine reports of the chairmen of the Council and of the various committees testify to this better than any listing here. And it shouldn't matter who thought it up, who did it or who gets the credit. As Emerson said, "My life is for itself and not for a spectacle." What does matter is what was accomplished—and the quality and quantity. Working with such alert people, considering each other's thoughts objectively in search for answers as nearly right as possible, has been a privilege in itself.

IV. Anticipation: Just recently we celebrated Easter and Passover, both of which commemorate the end of one form of life, and the beginning of another, better life. For some time we have been approaching a military crisis—in Vietnam. "The nation is in the midst of the worst financial crisis since 1931," so states Federal Reserve Board Chairman William McChesney Martin. A political crisis will reach its climax six months hence. Some say the health care of our people is nearing a crisis. Whether or not we agree with these conclusions, there must be some basis for them and some causative factor. It behooves us to consider the past life, and to be sure that the future will be a better one. Indeed, our presence here is witness to that goal. It is better that we find, or at least influence, a solution within our profession than to have one thrust upon us from without.

In this land where the quality of medical practice is so excellent, some people do not receive good health care. What are some of the reasons? Our committees on rural health and emergency medical service are seeking to shorten the miles and utilize the manpower more efficiently. Because some citizens find their health bills higher than they can afford, they avoid medical aid. Therefore, organized medicine is searching for ways to provide good care at diminished costs.

More complex is the problem in the densely populated poverty areas. Representatives of the Society are meeting with leaders in these areas, with the social workers, and with the poor themselves—to help determine the needs and the best way to fulfill them. Of great help to this cause can be such charitable organizations as the recently activated Hartford County Medical Foundation, financed by voluntary contributions and established to promote and help support educational and scientific projects related to health and medicine. But a long period of education will doubtless be necessary to overcome habit, apathy and fear.

The medical schools are also concerned with this matter. The Society has developed a much better—though far from adequate—relationship with them. We should move aggressively toward a closer incorporation of tomorrow's physicians into our Society through our own student members and the Student American Medical Association. Their indoctrination should come in large measure from the practicing physician, not just from the academician and theorist who has not had to cope with patients outside the sphere of a protective university hospital.

Tonight, our Committe on Medicine and Religion has arranged an amazing panel discussion on the "Changing Attitudes Toward Abortion and Contraception" at 8 o'clock. Where does life start —and end? We will discuss this afternoon in Reference Committee, recommendations for the abortion law. Three of our Committees are seeking to assist our members in how best to promote education in sex and in family life in the community. What about the chap who is made up of nothing but spare parts—and never really was born? We can no longer be just scientists. We must be part minister, part sociologist, part lawyer.

As such—and if we are to think ahead—we must help plan to train the citizen of tomorrow by training the youth of today. Oddly enough, in these days of supereducation, people receive almost no preparation for their most important job in life, bringing up tomorrow's adult: being a parent. That youth, that citizen, needs the security, the moral fiber, of high standards in those he looks up to. He needs gradually to develop self-discipline, a consciousness of and consideration for, his community. This responsibility lies with the parent—who needs help. If it is left to government, we proceed to a paternalistic state. And, two weeks ago in New Orleans, Solicitor General Erwin N. Griswold pointed up in the case of Spock and Coffin, the difference between the moral and legal right to disobedience. How can youth learn this in school when the mass of faculty disregards it?

Must we be content just to extricate barbiturates with the artifical kidney, institute psychotherapy, clean up after shootings, auto-wrecks and "trips"? No, it is our business as well to insist on working closely with educators to lay a stable personality foundation early in life and be responsible for erecting a sturdy super-structure as the formal schooling progresses. This is not an easy project, but neither was the cardiac transplant. And which will be more useful to mankind?

In our own Society, and in the American Medical Association, we must cultivate free and open discussion. Both organizations must represent, and therefore be run by, the individual membership—not in every detail of course, but the fundamentals must be thrashed out. The elected officials must feel the confidence of their electors, and a sense of unity must prevail.

The AMA is most helpful in co-ordinating the efforts and in making available background material. We must think clearly and objectively, plan what is right and work for that, not just accept extrinsic standards so as to qualify for grants and other powers. We need courage—to say what we believe today, "and tomorrow speak what tomorrow thinks in hard words again, though it contradict everything . . . said today." We must expend the energy to encourage and help the legislators who promote rationally the best interest of the entire public. And, further, we must contribute our dollars to our political arms—COMPAC and AMPAC—to get these people elected.

We have long sought for our people the best health care possible at a reasonable cost—today and tomorrow. If we pursue this course even more vigorously and wisely—and police our own house conscientiously—if every member works as a whole doctor, we will be happy and so will our patients.

It has been a pleasure and an honor, and a maturing experience to serve as your President. I hope I may be of some help to you still. Tomorrow Dr. Norman H. Gardner, our long-time Delegate to the AMA, will take over the reins. I know you will work as actively and faithfully with him as you have with me this past year. The wagon is rolling and is heavy laden. It will be guided well, but it needs your effort to keep it going. You won't be sorry. "Give, and it shall be given unto you."

Placement Wanted

INTERNIST—Board eligible resident in internal medicine at the New York Hospital desires association with established group or physicians in Fairfield County. Will be available July, 1968.

NEUROLOGIST—Board eligible, seeks clinical affiliation in Connecticut. Considerable experience in Internal Medicine, Neuropathology and Psychiatry. Connecticut license, military obligations satisfied.

PSYCHIATRIST—Board certified, 37 years of age, with extensive clinical and administrative experience, is interested in locating in Connecticut. Seeks (part-time) position in M.H. clinic or mental health center, in addition to private practice.

PSYCHIATRIST—NYU trained, Connecticut and New York licenses, seeks full or part time position in Connecticut.

RADIOLOGIST—40 years old, Chief, university radiotherapy department. New York, Connecticut licensed. Interested in private practice of radiotherapy in western Connecticut.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Doctor's Office

Harold Abrams, M.D., announces the opening of an office for the practice of general surgery at 881 Lafayette Street, Bridgeport.

Robert H. Berland, M.D., announces the opening of an office for the practice of neurology at 60 Gillett Street, Hartford.

HOUSE OF DELEGATES ADOPTS POLICY ON THERAPEUTIC ABORTION

Reproduced below is the statement of policy regarding thereapeutic abortion adopted by the CSMS House of Delegates on May 1, 1968, Immediately following the statement is reproduced an excerpt from the text of the Reference Committee report adopted by the AMA House of Delegates, Atlantic City, New Jersey, June, 1967, which, in part, constituted the basis for the statement adopted for the Society.

THE CONNECTICUT STATE MEDICAL SOCIETY STATEMENT OF POLICY RE. THERAPEUTIC ABORTION

(Approved by CSMS House of Delegates, May 1, 1968)

The Connecticut State Medical Society is cognizant of the fact that there is no consensus among physicians regarding the medical indications for therapeutic abortion. However, the majority of physicians believe that, in the light of recent advances in scientific medical knowledge, there may be substantial medical evidence brought forth in the evaluation of an occasional obstetric patient which would warrant the institution of therapeutic abortion either to safeguard the health or life of the patient, or to prevent the birth of a severely crippled, deformed or abnormal child.

Under these special circumstances, it is consistent with the policy of the Connecticut State Medical Society for a licensed physician (M.D.), in a hospital approved by the Commissioner of Health of Connecticut, and in consultation with two other physicians chosen because of their recognized professional competence who have examined the patient and have concurred in writing, to be permitted to prescribe and administer treatment for his patient commensurate with sound medical judgment and currently established scientific knowledge. Prior to the institution of a therapeutic abortion, the patient and her family should be fully advised of the medical implications and the possible untoward emotional and physical sequelae of the procedure.

In view of the above, and recognizing that there are many physicians who, on moral or religious grounds, oppose therapeutic abortion under any circumstances, the Connecticut State Medical Society recommends the revision of the Connecticut Statutes so as to permit the performance of therapeutic abortion when the following specific conditions are met:

1) There is documented medical evidence that continuance of the pregnancy may threaten the health or life of the mother, or
2) There is documented medical evidence that the infant may be born with incapacitating physical deformity or mental deficiency, or
3) There is documented medical evidence that continuance of a pregnancy, resulting from legally established statutory or forcible rape or incest, may constitute a threat to the mental or physical health of the patient, and
4) That, in any of the foregoing situations, any potentially dangerous physical or mental sequellae to the performance of therapeutic abortion have been carefully considered; and
5) Two other physicians chosen because of their recognized professional competence have examined the patient and have concurred in writing; and
6) A committee on therapeutic abortion of the hospital concerned has reviewed the written findings and opinions of the attending physician and of the two consulting physicians and has given prior written approval to the termination of pregnancy; and
7) The procedure is performed in a hospital approved for such procedure by the Commissioner of Health of the State of Connecticut.

It is to be considered consistent with the principles of ethics of the Connecticut State Medical Society for member physicians to provide medical information to the Connecticut General Assembly in its consideration of revision and/or the development of new legislation regarding therapeutic abortion.

House of Delegates, American Medical Associatior
Atlantic City, N.J.—June 18-22, 1968

Report F of The Board of Trustees—Therapeutic Abortion

This report transmits to the House, with the approval and recommendation of the Board, a detailed document and policy recommendation on therapeutic abortion prepared by the Committee on Human Reproduction. A previous report by that Committee on this subject was considered by the House in November 1965 at which time no action was taken pending further study. The present report represents an *in* depth study over a period of eighteen months in which all facets of the problem were explored.

Your Reference Committee heard voluminous testimony on this report. All points of view were expressed with the preponderance of testimony favoring the adoption of the recommendations. Almost without exception, those who spoke—both pro and con—commented on the excellence of the report. Your Reference Committee concurs in this viewpoint and wishes to commend the Board of Trustees and the Committee on Human Reproduction for the thoroughness with which they have explored this subject and for the temperate and impartial manner in which they have handled a very difficult subject.

In contrast to the 1965 report on this subject, the present report does not address itself to state abortion laws. It does propose updating of the 1871 policy statement by the American Medical Association. Your Reference Committee is in agreement that this 96-year-old policy should be revised; in our view, it is not only antiquated but lacks even the rudiments of adequate safeguards to prevent abuse. We believe that the updating of Association policy proposed in the present report is in keeping with modern scientific knowledge, contains necessary safeguards, and permits the physician to exercise his personal conscience and medical judgment in the best interest of his patient. These should be the overriding objectives in any medical decision.

Your Reference Committee recognizes, as does the Committee on Human Reproduction that there are many physicians who, on moral or religious grounds, oppose therapeutic abortion under any circumstances. The right of these physicians to express and practice their belief must be respected. This report in no way suggests that physicians or patients act contrary to their personal consciences.

In the opinion of your Reference Committee, and as brought out in the body of the report and in the testimony, there is unmistakable evidence of restiveness in all segments of the population regarding our current therapeutic abortion practices. It is clear that change and reform in this area is inevitable. The policy which this report recommends is a reasonable and conservative approach to the problem and one which, if adopted, will be consistent with the position of leadership of the American Medical Association.

Welcome, New Members

Hartford County Medical Association

Norman Alisberg, M.D., 2 Holcomb Street, Hartford, Conn. 06112.

John S. Bagnall, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Paul H. Barbour, M.D., 2 High Street, Farmington, Conn. 06032.

James C. Black, M.D., 1680 Albany Avenue, Hartford, Conn. 06105.

Robert C. Burchell, M.D., Hartford Hospital, Hartford, Conn. 06115.

Michael E. Carey, M.D., 287 Collins Street, Hartford, Conn. 06105.

John J. Curran, M.D., Institute of Living, Hartford, Conn. 06103.

John R. Gaintner, M.D., McCook Hospital, Hartford, Conn. 06112.

Herbert Gold, M.D., 99 Pratt Street, Hartford, Conn. 06103.

Joseph W. Healy, M.D., 51 Gillett Street, Hartford, Conn. 06105.

Mark W. Izard, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Edward J. Jarboe, M.D., 300 Kensington Avenue, New Britain, Conn. 06050.

Charles S. Kahn, M.D., New Britain General Hospital, New Britain, Conn. 06050.

Robert H. Kalinowski, M.D., 104 Lancaster Road, West Hartford, Conn. 06119.

David A. Lund, M.D., New Britain General Hospital, New Britain, Conn. 06050.

William P. Macaulay, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Barbara A. McLean, M.D., St. Francis Hospital, Hartford, Conn. 06105.

Sherwin Mellins, M.D., 79 Elm Street, Hartford, Conn. 06115.

Ali-Reza Mourizadeh, M.D., 73 Cedar Street, New Britain, Conn. 06052.

Herbert S. Pasternak, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Myron M. Pisetsky, M.D., 200 Retreat Avenue, Hartford, Conn. 06203.

George R. Walker, M.D., 79 Elm Street, Hartford, Conn. 06115.

Herbert J. Werner, M.D., 41 Jerome Avenue, Bloomfield, Conn. 06002.

John P. Wheeler, M.D., 36 Haynes Street, Manchester, Conn. 06040.

Barbara A. Witter, M.D., St. Francis Hospital, Hartford, Conn. 06105.

Fairfield County Medical Association

Anthony P. Borrelli, M.D., Danbury-Newtown Road, Newtown, Conn. 06470.

Norman M. Canter, M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.

Robert H. Craig, M.D., 35 Mason Street, Greenwich, Conn. 06830.

James P. Dudley, M.D., 49 Lake Avenue, Greenwich, Conn. 06830.

Arthur A. Echental, M.D., 98 Hoyt Street, Stamford, Conn. 06905.

Rafael D. Gonzalez, M.D., Danbury Hospital, Danbury, Conn. 06810.

Victor R. Grann, M.D., 98 Hoyt Street, Stamford, Conn. 06905.

Donald M. Haskins, M.D., 35 Mason Street, Greenwich, Conn. 06830.

William V. Healey, M.D., 49 Lake Avenue, Greenwich, Conn. 06830.

Einar A. Lundberg, M.D., 1937 West Main Street, Stamford, Conn. 06902.

David R. Mc Kee, M.D., 144 Morgan Street, Stamford, Conn. 06905.

Peter W. Pratt, M.D., 30 Hospital Avenue, Danbury, Conn. 06810.

Anthony P. Redmond, M.D., 49 Lake Avenue, Greenwich, Conn. 06830.

George H. Reichling, M.D., Main & Catoonah Streets, Ridgefield, Conn. 06877.

Thomas D. Rodda, M.D., 49 Lake Avenue, Greenwich, Conn. 06830.

Walter T. Shanley, M.D., 2660 Main Street, Bridgeport, Conn. 06606.

Douglas W. Thomas, M.D., Box 192, Newtown, Conn. 06470.

H. Norman Truax, M.D., Norwalk Hospital, Norwalk, Conn. 06850.

Howard E. Voss, M.D., 144 Morgan Street, Stamford, Conn. 06905.

Litchfield County Medical Association

Purificacion K. Pua, M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.

Richard Westsmith, M.D., Main Street, Lakeville, Conn. 06039.

Middlesex County Medical Association

Wayne B. Andrus, M.D., Stonegate Drive, Portland, Conn. 06480.

Hans O. Gerz, M.D., 75 Acer Drive, Middletown, Conn. 06457.

David B. Hickox, M.D., 33 Pleasant Street, Middletown, Conn. 06457.

Juan B. Sosa, M.D., Box 351, Middletown, Conn. 06457.

John B. Tompkins, M.D., 95 Marlborough Street, Portland, Conn. 06480.

New Haven County Medical Association

Alan Balsam, M.D., Dept. of Psych., Yale Med. School, New Haven, Conn. 06510.

Joseph W. Cooch, M.D., 2051 Bridgeport Avenue, Milford, Conn. 06460.

Edward L. Etkind, M.D., 1546 Chapel Street, New Haven, Conn. 06511.

Maurice Falk, M.D., 577 North Church Street, Naugatuck, Conn. 06770.

Douglas A. Farmer, M.D., 1450 Chapel Street, New Haven, Conn. 06511.

Richard E. Fearon, M.D., 2 Church Street South, New Haven, Conn. 06519.

Edward A. Jacobs, M.D., Yale New Haven Hospital, New Haven, Conn. 06504.

Edwin L. Lytle, M.D., Gaylord Hospital, Wallingford, Conn. 06494.

Gordon K. Mac Leod, M.D., 135 College Street, New Haven, Conn. 06510.

William F. Quigley, M.D., 29 Central Avenue, Waterbury, Conn. 06702.

Urmila C. Shah, M.D., 666 George Street, New Haven, Conn. 06511.

Richard M. Swengel, M.D., 789 Howard Avenue, New Haven, Conn. 06504.

Leland W. Wight, Jr., M.D., Yale New Haven Hospital, New Haven, Conn. 06504.

Ormond L. Wilkie, M.D., Gaylord Hospital, Wallingford, Conn. 06494.

Theodore Zanker, M.D., 315 Whitney Avenue, New Haven, Conn. 06511.

Leon Zucker, M.D., 29 Central Avenue, Waterbury, Conn. 06702.

New London County Medical Association

David C. Marshall, M.D., 154 Broad Street, New London, Conn. 06320.

Daniel E. Moalli, M.D., 350 Montauk Avenue, New London, Conn. 06320.

Mario J. Sculco, M.D., 257 Main Street, Norwich, Conn. 06360.

Lyman E. Sproul, M.D., Sandy Hollow Road, Mystic, Conn. 06355.

Djin L. Tan, M.D., Norwich Hospital, Norwich, Conn. 06360.

K. Stephens Taylor, M.D., 161 Water Street, Norwich, Conn. 06360.

John W. Troy, M.D., Medical Arts Building, Gales Ferry, Conn. 06335.

Christian D. van der Velde, M.D., Box 508, Norwich, Conn. 06360.

Griffith J. Winthrop, M.D., 21 East Main Street, Mystic, Conn. 06355.

Windham County Medical Association

Maurice R. Harton, M.D., 11 Spring Street, Danielson, Conn. 06239.

CHANGES OF ADDRESS

Notice of change of address should be sent not less than four weeks prior to the date the change becomes effective. Please send the address label from one of the issues you've just received, which shows code numbers to help us make the change promptly, along with the new address and your *zip code.*

CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut, 06511

when you want to provide the combined benefits of two accepted agents in the treatment of mild to moderate hypertension. (Contraindications: history of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.)

when you want to prescribe therapy that is generally well tolerated. (However, adverse reactions may occur. For a complete listing, please refer to the full prescribing information which is summarized below.)

when your patient wants an easy-to-remember and reasonably priced regimen. (One tablet a day usually costs about a dime.)

Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue 1 week before electroshock therapy, and if depression or peptic ulcer occurs. **Use in pregnancy:** Regroton should be used in pregnant patients or in women of childbearing potential only when, in the judgment of a physician, its use is deemed essential to the welfare of the patients; adverse reactions (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn. **Precautions:** Antihypertensive therapy with Regroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue Regroton therapy two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Regroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angiitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. **For details, see complete Prescribing Information.** (B)46-600-B

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OBITUARIES

ARTHUR BLAND SULLIVAN, M.D.

1911 - 1968

Dr. Arthur Bland Sullivan of West Hartford died at the Hartford Hospital on March 8, 1968, of a dissecting aortic aneurysm.

Born December 2, 1911, in Hartford, Connecticut, the son of Robert J. Sullivan and Mary Bresnahan Sullivan, he was a graduate of William Hall High School, Harvard University, Class of 1934, and Yale Medical School, Class of 1938. After interning at Hartford Hospital, he practiced general medicine in the greater Hartford area for twenty-two years. He served five years in the United States Medical Corps during World War II with more than three years overseas duty in Iceland and England, and was discharged as a major in 1946.

Dr. Sullivan was a member of the assistant staff of the Hartford Hospital in the Department of Medicine, on the courtesy staff of Saint Francis and Mount Sinai Hospitals, and served as a consultant physician at Saint Mary's Home, West Hartford. He was a member of the Hartford Medical Society, Connecticut State Medical Society, and the American Medical Association; was president of the Medical Advisory Board of Saint Mary's Home and a member of the Professional Advisory Committee of the Visiting Nurse' Association.

"Archie," as we all called him, devoted his life to his wonderful family and his practice as a family doctor. He was a man of sincere religious convictions; he was marked by integrity, firmness, gentleness and humility. His sense of humor and enjoyment of life endeared him to his many friends.

He leaves his wife, Mrs. Patricia Deming Sullivan; four sons, Brian, Craig, Gerald and Arthur Jr.; three daughters, Janice, Elizabeth and Evelyn; his mother, three brothers and five sisters.

Edward J. Conway, m.d.

BURNHARDT ZEMAN, M.D.

1882 - 1968

Dr. Burnhardt Zeman of 296 North Quaker Lane, West Hartford, Connecticut, a member of the Hartford County Medical Society, Connecticut State Medical Society and the American Medical Association for many years, died on March 26, 1968 at St. Francis Hospital, Hartford.

Dr. Zeman was born in Russia and received his secondary education at the Gymnasium. He obtained his pre-medical education at the University at Konigsberg, Germany, and came to the United States in 1903. In 1908 he graduated from the Kentucky School of Medicine, which is now the University of Louisville, School of Medicine, where he obtained his medical degree. He interned at the Maryland General Hospital in Baltimore, Maryland and then came to Hartford, where he established practice He practiced in the greater Hartford area from that time until two years ago when he retired. He was one of the founders of the Mt. Sinai Hospital and served for many years on the staff of Mt. Sinai Hospital. At the time of the founding of the hospital, he was for several years the Chief of the Department of Radiology.

His wife, the late Annie Saxe Zeman, was a prominent woman in the Hartford community in both its social and communal life.

Dr. Zeman is survived by two sons, Dr. Michael S. Zeman of Louisville, Kentucky, an otolaryngologist, who formerly practiced in Hartford, and Attorney William S. Zeman of West Hartford, five grandchildren and two great-grandchildren. His grandson, Dr. Peter Michael Zeman is an intern at Hartford Hospital and will commence a three year residency at the Institute For Living in July.

Michael S. Zeman, M.D.

In Memoriam

Flynn, Herbert L.—Mansfield Depot; University of Vermont College of Medicine, 1929. Dr. Flynn was a practicing psychiatrist for over 20 years. He had served in World War II and was a reserve officer for 22 years. Dr. Flynn was assistant superintendent at the Mansfield Training School. He was a member of the Windham County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American Psychiatry Association, and the New England and the Connecticut District Branch of the American Psychiatry Association. Dr. Flynn died January 1, at the age of 66.

Moriarty, Mortimer E.—Manchester; Yale University School of Medicine, 1926. Dr. Moriarty had practiced in New Britain for 40 years. He was a World War I Army veteran. Dr. Moriarty was a former chief of medicine and senior physician of the medical staff at the Manchester Memorial Hospital. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Moriarty died May 2, at the age of 70.

Powers, Grover F.—Hamden; Johns Hopkins Medical School, 1913. Dr. Powers was a professor emeritus of pediatrics at the Yale School of Medicine. For his contributions in the field of mentally retarded children, Dr. Powers received the Joseph P. Kennedy Jr. Award, the Borden Award, the Howland Medal and Award, and many others. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American Academy of Pediatrics, the American Pediatric Society, the Society for Pediatric Research, the Society for Experimental Biology and Medicine, and the Society for Clinical Investigation. Dr. Powers died April 10, at the age of 80.

Satti, John C.—New London; Yale School of Medicine, 1923. Dr. Satti was a general practitioner for over 40 years. He served as Connecticut's Secretary of State for two terms, 1934 to 1938. He was Democratic state central committeeman for 16 years and town chairman for his native New London for 24 years. Dr. Satti was a former president of the National Association of Secretaries of State. He was a member of the New London County Medical Association and the Connecticut State Medical Society. Dr. Satti died May 7, at the age of 72.

COMMENTS ON THE 1968 CONNECTICUT PHYSICIAN'S ART EXHIBIT

In general, the Art Exhibit seemed well received again this year. There were 71 art works entered, and the facilities for displaying this exhibit were improved over last year. The art work included a wider range of media this year. This was especially true in the sculpture section.

The awards given were as follows:

"BEST IN SHOW" went to Dr. William Schneider of Rockville for an acrylic painting entitled "Harbor."

JOHN M. FREIHEIT AWARD went to Dr. Robert Lowman of New Haven for an oil painting entitled "Vineyard Winter—Jeffers Barn."

In the professional category the first prize was won by Mrs. Ruth Waskowitz of Kensington for a water color entitled "Guppies."

Second Prize to Dr. Sophie Trent of Meriden for a collage entitled "Abstract in Blue."

Honorable Mention is this category went to Mrs. Ruby Gilman of Storrs for an oil painting entitled "Sundrenched."

Water Color:

First Prize went to Mrs. Liesel Braun of Trumbull for a picture entitled "Colorado Peak."

Second Prize to Mark Hayes, Jr., of North Haven for a painting entitled "Exercise #1."

Honorable Mention to Dr. Donald Morrison of West Hartford for a painting entitled "Solama."

Black & White Category:

First Prize went to Mrs. Teresa D'Esopo Onsager of Hamden for a drawing entitled "Mule Deer."

Second Prize went to Justin Gordon of Hartford for an ink drawing entitled "In the Still of the Night." (father Yale Gordon, M.D.)

Sculpture—Intermediate Category:

First Prize to Mrs. Philip Nelson of New Canaan for a bronze cast entitled "Selina." (father E. Tremain Bradley, M.D.)

Second Prize to Mrs. Samuel Rentsch of Derby for a stone carving entitled "A Cloud."

Honorable Mention to Richard Shaw, M.D. of West Hartford for a metal sculpture entitled "Still Life #1."

Sculpture—Beginners Category:

First Prize to Mrs. Patricia McDermott of Bristol entitled "Indian Head"—stone.

Second Prize to Henry B. Low, M.D. of Hartford entitled "Heart"—stone.

Honorable Mention to Orvan W. Hess, M.D. of New Haven entitled "Wellfleet Whale"—clay.

Honorable Mention to Mrs. Patricia McDermott of Bristol entitled "Self Portrait"—fiberglass.

Photography:

First Prize went to John A. Woodworth, M.D. of Moosup for "Old Man Wood."

Continued on page 489

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ANNUAL REPORT OF THE PRESIDENT — 1967-1968

No account of my stewardship in office can be complete without reference to the powerful political and social forces which, in terrible ferment, have affected and continue to threaten society and the medical profession.

What affects society, whether it be the spread of ghettoes, or drug abuse or illegitimacy, affects us as an Auxiliary because the medical profession is ultimately involved. If these problems are not tackled at the local level, it is not difficult to forecast that the Federal Government will step in with a host of new programs, including national health programs.

As Auxiliary members we must be concerned with the concerns of our citizens—and that means striking out in new directions. Helping the poor, maybe, or trying to promote recial peace in the community. Above all, it means educating ourselves and educating others to the needs of our times.

The Auxiliary is in a unique position to achieve this goal. By informing its members the Auxiliary can inform other doctors' wives at the local level. Through the delegate system, to which we belong, the Auxiliary can influence the activities of the Connecticut Health Careers Council, the Nutrition Council, the Connecticut Health League, the Connecticut Advisory School Health Council, and of course, COMPAC. We have active members on both the State and National boards of these councils.

In all this liaison work, the objectives of the Society and the Auxiliary work are uppermost. Nevertheless, I believe there is still room for discussion of society's current problems.

Our objectives as an Auxiliary—community service, education, and support for the medical profession—were admirably filled this past year. And for this wonderful record, my deepest thanks to our hard-working committee chairmen and to the dedicated members.

Let me touch on some of the highlights. Programs were conducted by various county auxiliaries on the dangers of quackery. Emergency Medical Cards were distributed at several rural fairs. Countless hours of volunteer service have been given by our members to the Pre-School Visual Screening Program, to distribution of kits during Diabetes Detection Week, to Meals on Wheels—our first ventur in the ghetto areas, to the Red Cross Bloodmobile, to the "Help Line" from the Connecticut Valley Hospital, and to Coffee Hours for the mentally ill at the Veterans' Hospital.

Our humanitarian service does not stop at the shore line. Auxiliary members have created international goodwill by making Johnny Coats and leper badges for use abroad. Medical and nursing books and medical instruments, slightly used in good condition, have been collected and sent abroad Medical and nursing books and medical instruments, slightly used but in good condition, have been collected and sent abroad for use in underdeveloped countries.

In the same vein but on a person-to-person basis, one of our past presidents, a speech therapist, has initiated a program of devoting one night a week to helping foregn interns brush up on their English. This is a rewarding and worthwhile project and it deserves the support of other Auxiliary members. I don't have to remind you that a program of this sort also helps our husbands.

The health careers recruiting program continued to receive wide support in the countries this past year. Health careers programs, featuring films and speakers, were conducted in 30 schools. The programs were effective, opening the eyes of many

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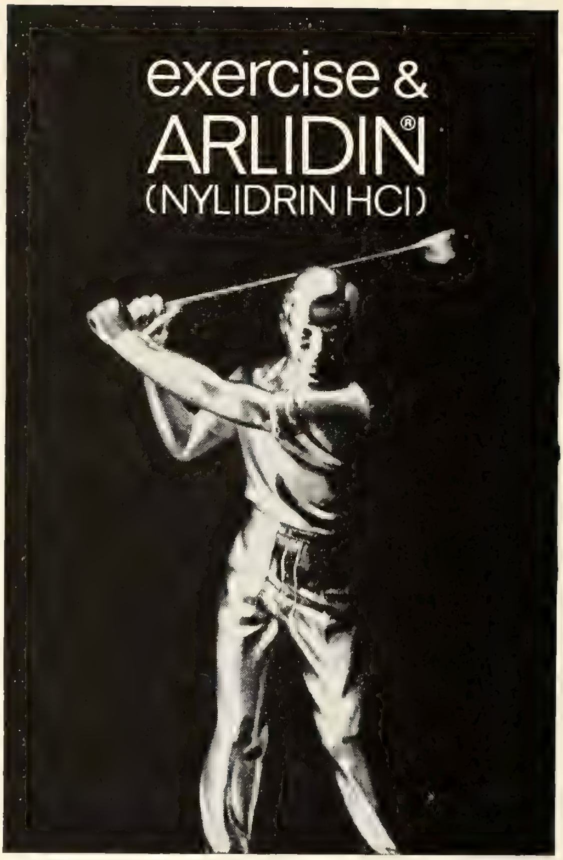

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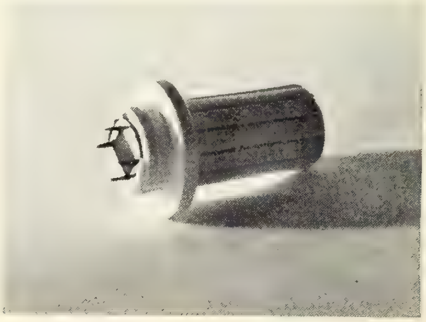

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students to opportunities which they were unaware existed in Medicine.

Our find raising activities deserve mention. Through dances, card parties, and so forth, the counties were able to award 25 scholarships valued at $6,000 to young people pursuing health careers in Medicine, Nursing, Technology, Speech Therapy, and Immunology. Similar undertakings succeeded in reaising $3,000 for the American Medical Association's Education and Research Foundation. That sum brings total contributions in eight years to $25,000. The Auxiliary has a right to be proud of its work!!

Legislation naturally continues to be a major concern of ours. Over 1,600 health bills were filed in the Connecticut eneral Assembly last year. The AMA estimates that well over 5,000 health bills have been introduced in the current session of Congress. Needless to say, the bulk of those bills favor xpansion of existing health care programs and, as such, chip away at the private sector of medicine. With the state and national elections just a few months away, it is necessary for women every where to work for the party of their choice, to join COMPAC, and to be a part of our changing times. Our Safety Chairman has joined hands with legislation to investigate the sale of eyeglasses without prescriptions.

The editors of the "The Quarterly" have done a spledid job of informing the members of the Auxiliary's activities. If anyone asks, new and old members, "What does the Auxiliary do?" They need only read "The Quaterly." The answers are found in its pages. The reader will come to apprciate not only what the Auxiliary does but also the excellent camaraderie its members share and enjoy.

So much for the record. Let me speak briefly about tomorrow. As I mentioned at the House of Delegates, the Auxiliary's 25th anniversary observance is a watershed. In recalling our accomplishments, we also have an opportunity to chart our course for the future, guided by a commitment to work toward solutions of the problems which threaten our society and, as a consequence, the foundations of the medical profession.

The drop in our membership to 993 has certainly distressed us. Fairfield County's efforts to reactivate itself, however, should refurbish our membership.

(Mrs. Anthony P.) Marguerite Cipriano
President

Art Exhibition, Continued from page 485

Second Prize went Rudolph Braun, M.D. of Trumbull for "Pelicans."

Honorable Mention to John A. Woodworth, M.D. of Moosup for "Cap'n Tuttle's Home Port."

Oil Beginners:

First Prize went to Mrs. Alberta Glassman of Branford for "Self Portrait."

Second Prize went to Mrs. Ann Murphy of West Hartford for "Up, Up and Away."

Second Prize also went to Robert Husgar, M.D. of Hartford for "Eagle."

Honorable Mention went to Greg Shoukimas of West Hartford for "Untitled." (father John Shoukimas, M.D.)

Oil Intermediate:

First Prize went to Herman Austrian, M.D., of Trumbull for "Still Life."

Second Prize went to Stewart Petrie, M.D., of Seymour for "Roman Forum."

Honorable Mention went to Mrs. Stanley Brodoff of New Haven for a primitive painting entitled "The Perrottis."

Children Category:

First Prize went to Wendy Fairlie of West Hartford for an old painting entitled "Untitled." (father C. W. Fairlie, M.D.)

Second Prize went to Harold Gordon of West Hartford for a Batik entitled "Life." (father Yale Gordon, M.D.)

Honorable Mention went to Cara Sonnen of Somers for an old painting entitled "My House." (father Victor Sonnen, M.D.)

The judges were:

Gail W. Martin—Prof. of Art—Hartford Art School of the University of Hartford, Member—Connecticut Water Color Society and Connecticut Academy of Fine Arts.

Mitchell Pappas—Associate Professor of Fine Arts—Trinity College. Member—Connecticut Water Color Society and Connecticut Academy of Fine Arts.

Ethel Stauffer—Hamden Painter & Teacher—Past President, New Haven Paint & Clay Club, also member Connecticut Academy of Fine Arts, and Pennsylvania Academy of Fine Arts.

The Art Association wishes to thank all those concerned especially the Connecticut State Medical Society, and Woman's Auxiliary, and a thank you is also extended to the New Haven County Medical Association for their presentation of the "Freiheit Award." A special note of thanks is extended to Mrs. John Shoukimas, Art Chairman, Woman's Auxiliary, Connecticut State Medical Society, West Hartford and her committee. It should be known, that the Art Committee is quite receptive to any suggestions regarding improvement of the show and its format. It seems to be the feeling of the Art Association, as well as many others, that interest and attendance at the State Society meeting is improved by this Art Show.

STEWART J. PETRIE, M.D. *President*
Connecticut Physicians Art Association

MRS. ORVAN W. HESS, M.D., *Vice-president*
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Connecticut Medicine

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Volume 32/July 1968/Number 7

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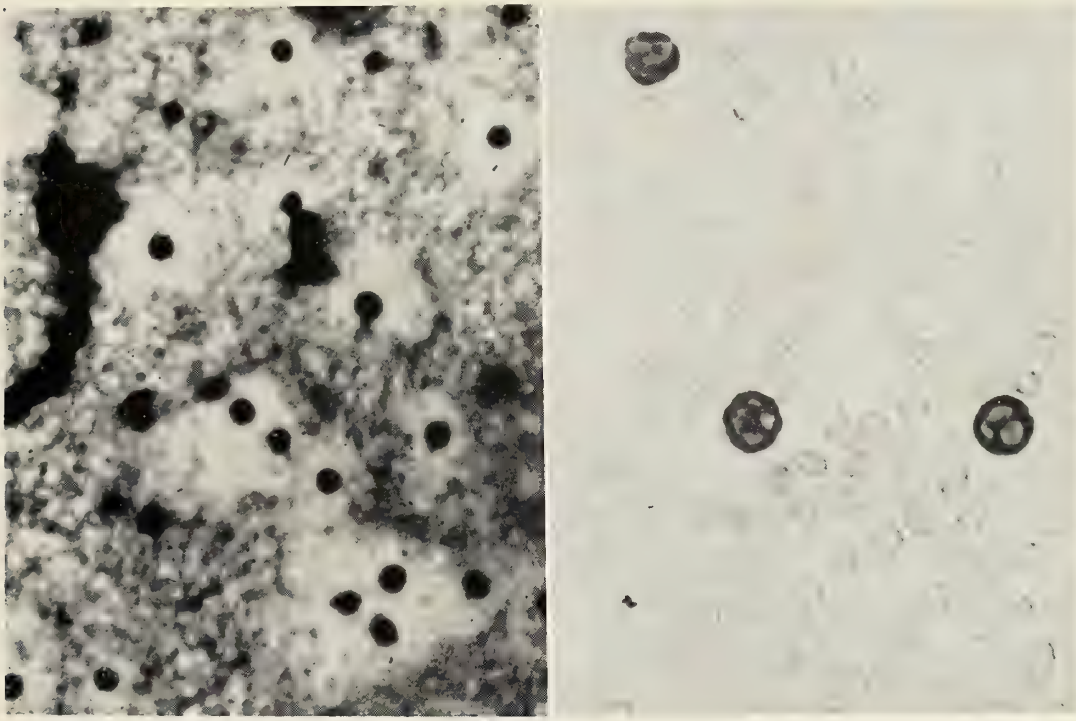

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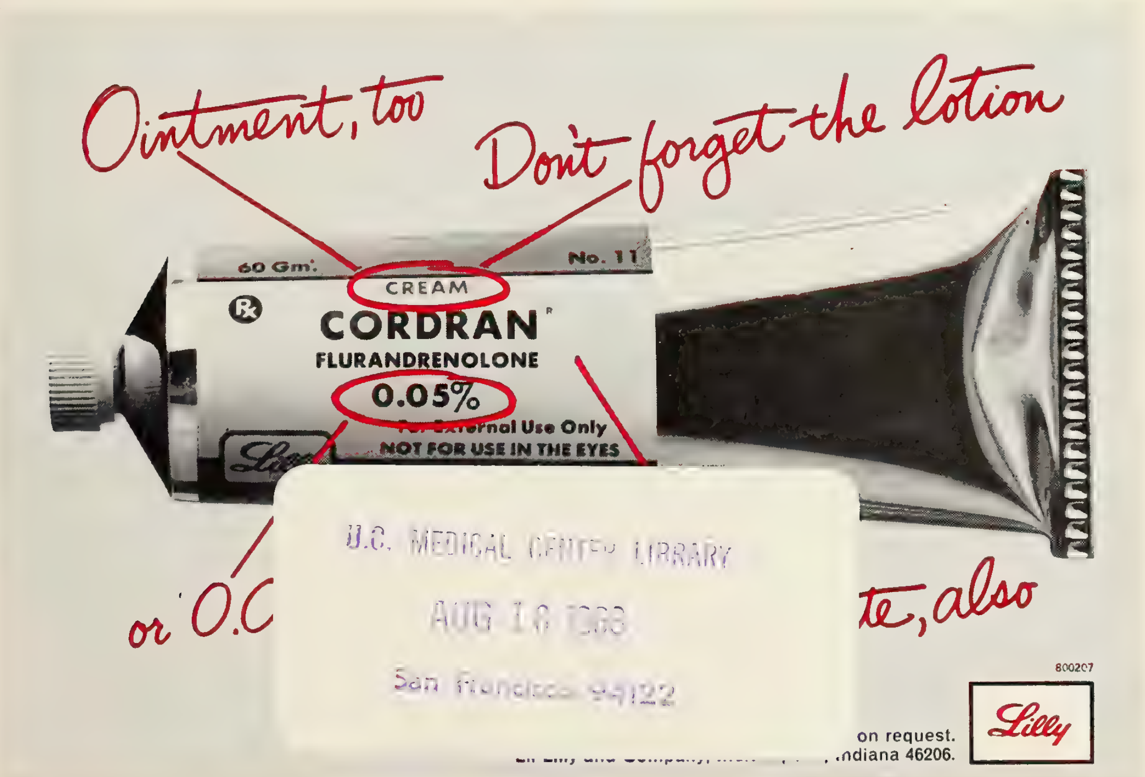

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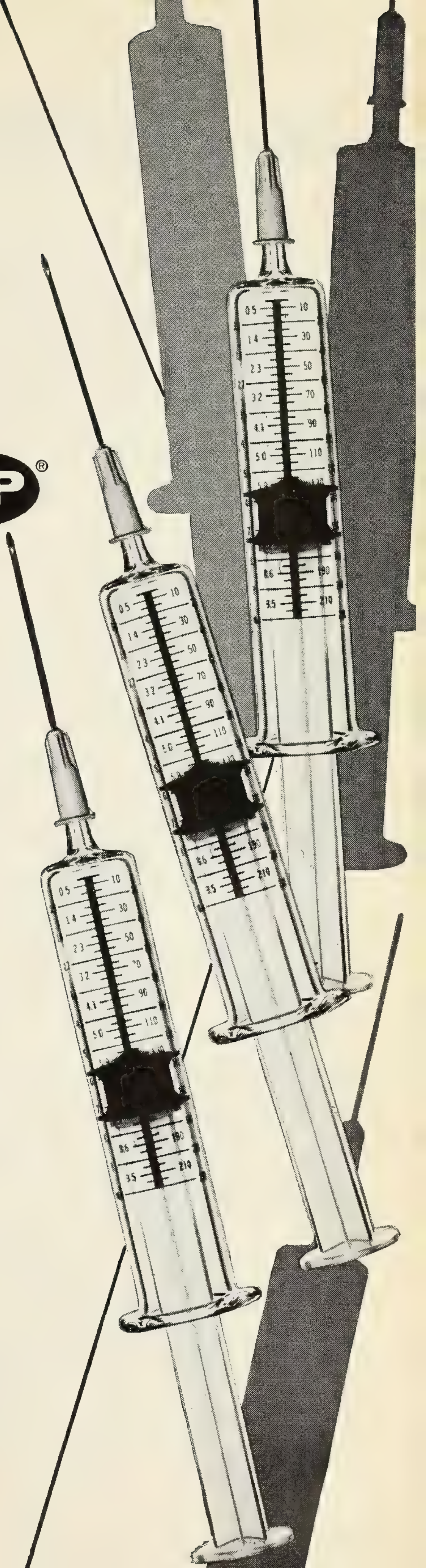

Connecticut Medicine

JULY, 1968
Vol. 32/No. 7

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Connecticut Medicine

editorials

The Bacterial Killing Process Of Polymorphonuclear Leucocytes

There are two metabolic characteristics of phagocytosis by normal cells One is greatly increased respiration during phagocytosis. The other is a stimulation equivalent to the amount of glucose that is passed into the polymorphonuclear leucocyte cell membrane through the hexose monophosphate shunt. Characteristic neutrophilic granules of normal cells release their hydrolytic enzyme when the cell ingests solid objects. The polymorphonuclear leucocytes in chronic granulomatous disease show a fundamental malfunction. The ingestion of external objects by the cells is normal. However, the ability of the leucocyte to kill the ingested bacteria is severaly depressed. Furthermore the respiratory response is also inhibited. How does this defect in bactericidal capacity of leucocytes for staphylococci come about? Quie, et al[1] have studied the leucocytes of patients in this disease. They determined leucocyte oxygen uptake during phagocytosis by an oxygen electrode in one case and by use of a Warburg respirometer in the other. Radioactive glucose oxidation was also studied in their first case during phagocytosis. The respiratory studies were performed on two female patients. In each case there was as noted above a fundamental malfunction of the leucocytes. The respiratory response of the cells was greatly reduced and the authors concluded that the leucocytes in this disease have a defective bactericidal capacity and show little oxygen uptake and little glycolysis.

Another way of studying the defect in the leucocytes of chronic granulomatous disease was employed by Bachner and Nathan[2] the quantitative nitroblue tetrazolium test. In studying the respiratory response of leucocytes during phagocytosis in this disease, it was noted that the cells failed to reduce nitroblue tetrazolium (NBT). It was then proposed that the quantitative NBT test would be used to detect such patients and even female carriers. Bachner and Nathan have now reported that the rate of reduction of NBT by normal leucocytes is stimulated by phagocytosis. It also depends on cell number, pH., and temperature.

Granulocytes of affected male patients failed to reduce NBT to blue formazan during phagocytosis, whereas leucocytes of carrier females usually asymptomatic demonstrated intermediate dye reduction. A seventeen year old girl with lifelong recurrent suppurative infections was identified as having chronic granulomatous disease by this method. Her leucocytes much as those of affected males had absent dye reduction, low values for oxygen consumption and diminished oxygen activity during phagocytosis. Her parents leucocytes had normal dye reduction rather than the intermediate values noted in mothers of affected males. In females the disease appears to represent a different form of genetic transmission than in the male.[3] Either it

THE COVER

The two low power photomicrographs on the cover demonstrate histologic techniques which are of value in leukemia diagnosis (see this issue—"Some Enzyme Changes of Clinical Importance in Leukemia" by Kaplow, Finch and Bertino). The photomicrograph on the left shows monoblasts from the peripheral blood of a patient with monocytic leukemia surrounded by clear zones of partially lysed bacteria *(M. lysodeicticus).* Leakage of lysozyme from the immature monocytes produces destruction of bacterial cell walls resulting in the halo or bull's eye effect. Myeloblasts and lymphoblasts contain little or none of this enzyme. The photomicrograph on the right shows an alkaline phosphatase stain of three neutrophils in the blood smear of a patient with a bacterial infection. The alkaline phosphatase presents as dense, dark cytoplasmic granules. In chronic myelogenous leukemia leukocyte alkaline phosphatase is greatly reduced in contrast to infection and other myeloproliferative disorders which usually are identified by normal or increased leukocyte enzyme content.

is a mutation, an acquired defect or else it is transmitted as an autosomal recessive trait.

If we are dealing with a genetic aspect in chronic granulomatous disease the thought arises that perhaps there is an absence of an enzyme. If not actually missing there could be an alteration of an enzyme which now has different regulatory characteristics from the normal enzyme. On the other hand the cause might be a modification of the cell membrane or the membrane surrounding the granules.

If the lesion were found to be in the metabolic machinery itself,[4] one might think that the degranulation follows metabolic changes set in motion by phagocytosis. On the other hand if the membrane itself is altered in the cells from patients with the disease then the metabolic alterations could be secondary to the membrane movements and changes that take place during phagocytosis. Thus there remain to be established the sequences in the process of metabolic stimulation of degranulation and of bacterial killing.

Before the disease was described in females, it was easy to think of one protein enzyme to be the key to the situation in the male victims. Now that the heretofore believed sex-linked disease can appear in females and most notably where no family history of the occurrence of this disease is evident, and where the members of the family show normally functioning leucocytes, the nature of the disease has become more complex. At least we can now say that a method is available for studying leucocytes at the metabolic level and by these methods investigators have been able to recognize a specific disease with increased precision.

L.H.N.

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An Approach To The Treatment Of Osteoporosis

Like every tissue bone is in a constant process of renewal with a physiological equilibrium maintained between calcium deposition and resorption. In osteoporosis bone removal proceeds more rapidly and intensively than bone deposition. Haas[1] points out that 1 osteoclast is as active as 100-150 osteoblasts. Obviously there is intensified bone turnover normally and in osteoporosis calcium deposition does not keep pace with increased rate of resorption. The clinicians difficulty is that by the time osteoporosis is clinically manifest or shows up in a radiograph it is already far advanced, nor is there any indication whether the disease process is active or halted.[2]

In principle the therapeutic approach to osteoporosis should seek either to inhibit bone resorption or try to promote bone deposition thereby achieving a genuine repair. Several substances are known to inhibit bone resorption. One is calcium if it is deficient in the diet because of malutrition malabsorption such as occurs after gastrectomy or in excessive calciuria. If the calcium balance is negative it tends to depress serum calcium, and this leads to increased production of parathormone which in turn causes abnormally high bone resorption. In such case high doses of calcium will serve to replenish the mineral reserviors. One will thetn find increased alkaline phosphatase levels, increased retention of calcium in skeleton and relief of the patients backache and diminished numbers of fractures. The simultaneous use of phosphates is still under trial.

Estrogens clearly inhibit osteoclasts in animal experiments. In human beings they lead to clinical improvement and reestablishment of calcium balance. Another substance which inhibits removal of calcium from skeleton is thyrocalcitonin.[3] Very few studies have been made of its short term effects in human beings largely because it has not been available in sufficient quantities. We may expect a definite answer as to whether this hormone has a place in treatment of osteoporosis now that it has been synthesized in a biologically active form by Bell and Anderson in Lederle laboratories. Thyrocalcitonin antagonizes parathormone which tends to draw calcium out of bones. It is therefore considered to be of use in the maintenance of the skeleton and should be therapeutically valuable in various types of osteoporosis, Paget's disease, hyperthyroidism and that due to chronically bed ridden patients.

There are several substances which promote bone growth in contrast to those mentioned above that prevent calcium loss from bone. Some like androgens stimulate osteoblastic activity. Growth hormone can stimulate osteoblasts but only very limited quantities are available for experimental trials. Fluoride apparently initiates a two phase process. At first there is a massive increase in alkaline phosphatase, but then after a while calcification develops in the newly formed osteoid tissue and a genuine if not complete repair process is started. Fluorine is so far the only substance we know which has a profound effect on bone deposition in the elderly patient. Osteoporosis is not known in populations who drink water with a high fluorine content. However, since fluoride treatment to be effective requires massive doses, some caution is urged by those who point out that too little is as yet known about its side effects. Finally there is vitamin D needed for calcium absorption in malabsorption syndromes and rickets.

There is one important factor in osteoporosis and that is inactivity. Mechanical stresses and strains are physiological factors operating to prevent bone resorption, and this includes use of gravity. In the absence of these two factors bone renewal does not take place and rapidly progressive atrophy through disease will aggravate the existing osteoporosis and not infrequently render it entirely refactory to treatment. Surgeons and physiotherapists are utilizing these principles in patients with fractures. They begin to apply systematic muscle training soon in vertebral fractures. They use pinning in fractures of the femoral neck to permit early ambulation and systematic training.

Where the cause of osteoporosis is known it must be eliminated. If it is not due to disease, intensive physiotherapy is mandatory. If due to steroids, bone recovers readily when steroids are withdrawn. If the patient has an elevated bone turnover evidenced by a high serum alkaline phosphatase, hypercalciuria and decreased retention of skeletal calcium then large doses of calcium for long periods are necessary. In general such treatment is well tolerated and concomitant constipation can readily be overcome.

If the patient is in the menopause, calcium plus estrogen and some androgen may be the best approach. When there are signs of a low bone turnover with a normal alkaline phosphatase low skeletal calcium retention and normal urinary calcium excretion Haas recommends small doses of estrogen and androgen combined without supplemented calcium. When all these methods are combined with physiotherapy measures one frequently obtains satisfactory clinical results.

We are learning much about bone metabolism. Increased alkaline phosphatase represent increased bone turnover. This is reinforced by values of calcium in the blood and amounts excreted in the urine. When thyrocalcitonin becomes available for clinical trial in the near future we will have another hormone to assist in stabilization of bone and prevention of osteoporosis.

L.H.N.

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Circum Corneae (Arcus Senilis)

The fatty arcus serilis is of no moment in the diagnosis of fatty heart.—Sir William Osler

Our knowledge on the etiology of "arcus senilis" is vague as witness Duke-Elder's statement. "It would seem most probable that the etiology is composite, the phenomenon being essentially determined by senile changes in the structure and metabolism of the cornea accentuated and accelerated sometimes by degenerative processes in the perilimbic circulation; sometimes by a decrease in the lipidolytic capacity of the serum and sometimes by anomalies in the metabolism of lipids which favor their deposition in quantity."[2] What a plethora of words and a paucity of ideas.

Some individuals show an apparently benign whitish ring around the scleral margin of the cornea. They have been described to occur at any age even at birth but is frequently observed in aged men and is commonly called "arcus senilis" even though it is neither an arc but a circle and even though it occurs at all ages and not only in old age. For these reasons it could better be termed "circum corneae."

Several investigators have suggested that the corneal ring is associated with arteriosclerosis and even myocardial infarction. The corneal deposit is made up of cholesterol, phospholipid and triglycerides as determined by histochemical and biochemical studies, substances that are also found in atherosclerotic plaques. Others, however, have denied any relation of the corneal deposit to vascular disease. In fact Macaraeg et al[3] have been struck by the higher prevalence of the corneal deposit in the negro especially the young negro. Accordingly they undertook a survey of two groups of American negroes and whites for the purpose of quantifying the prevalence of corneal deposits in various decades of life and of correlating its occurrence with diastolic hypertension, coronary heart disease, cerebrovascular accidents and elevated fasting blood sugar.

They found that the probability of any patient showing the corneal ring is related to both age and race. The older patient whether white or black is not only more likely to possess a corneal ring but the lesion is more advanced than in the case of younger patients. The black men and women begin to show the corneal ring at an earlier age than do their white counterparts and also have more advanced lesions for any given decade. Likewise the black man showed lesions at an earlier age than did the black woman. In the white patients the difference between the sexes was not so marked. This same result was confirmed in two different populations studied. To avoid the error of studying the corneal ring in a hospital population which is complicated by disease as well as socio-economic variables, the survey was carried out among employees of the Bethlehem Steel Corporation where the subjects are economically comparable, not hospitalized and free from serious illness. Thus their results apply to a general population.

Macaraeg's figures support the thesis that "arcus senilis" in incorrectly labelled senilis because of its occurrence also at early ages and further that its presence is not a careful predictor of degenerative vascular disease such as myocardial infarction, strokes and hypertension. Their data agree with a reported high incidence of atherosclerosis in African blacks and the Bantus who like the Aleuts may show the ocular lesion in the presence of low serum cholesterol levels and a low incidence of coronary heart disease. The black man is more likely to develop hypertension than the white but this phenomenon seems independent of his tendency to develop the corneal ring.

The postulated relationship between the corneal ring and atherosclerosis would seem to represent a confusion generated by the fact that two unrelated phenomena, the corneal ring and vascular disease are both more common in the older age groups. A high incidence of corneal ring has been generally described in essential familial hypercholesterolemia (EFH) but Wilkinson el al[4] found only one case and that in a person with normal cholesterol in 282 individuals comprising four generations with EFH. There also appears to be no relationship between the "ring" and secondary types of hypercholesterolemia such as occurs in diabetes mellitus, lipid nephrosis and myxedema.

The cause of the corneal ring remains a mystery. Many bizarre explanations have been offered without any warrant, from "dryness of the part" deposit of lymph formed by chronic inflammation, senescent vessels that poured out an opaque substance, sign of old age due to atherosclerosis, defective nutrition has been invoked as a cause and especially vitamin C deficiency, but none have been substantiated.

The absence of any definitive explanation of the circum corneae suggests a genetic basis for this lesion. In fact many have indeed claimed that hereditary factors are important. In juvenile "arcus" twins have been found to develop the condition in a similar form at the same age. Some like Stephenson[5] claim a dominant inheritance because he found 21 affected individuals out of 32 in 4 generations with blue sclera. There is no doubt that our knowledge about the etiology of Circum Corneae is vague but at least we known that the "arcus" is a ring and the lesion is not so "senilis."

L.H.N.

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Anti-Water Pollution Laws Need Interpretation And Correct Implementation

The U.S. Department of the Interior[1] is the custodian of the federal anti-water pollution program. The water quality act of 1965 called for effective state water quality standards which once approved by Interior would become the federal standards. The idea was to require imposed water quality on polluted streams and the protection of unpolluted waters. Interior was to be guided by the standards

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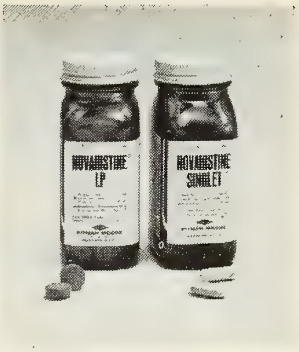

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of its own National Technical Advisory Commission on Water Quality Requirements for fishes or aquatic life and wildlife.

However, the water quality standards which Interior had aproved for Alabama and other states included standards for dissolved oxygen and water temperatures that did not meet the recommendation of its own advisory commission.[1] It accepted guidelines for water treatment that would remove heavy metals which are extremely toxic to aquatic environment. It accepted, however, water treatment that would not remove fertilizing chemicals which account for algae and other oxygen depleting growth which adversely affect water quality. It did not even consider thermal pollution. With such standards the accumulative effects of several plants can completely degrade a stream and ruin it for most beneficial uses.

The Interior policy represented an important retreat from the original basic concept: that polluters would eventually be required to construct whatever treatment facilities are necessary to keep water pure enough for all legitimate water uses. In such a situation who was Interior really serving, the public or the private interests who were not concerned with public welfare but merely to save money.

Had it not been for the National Wildlife Federation, the public would not have known that in the implementation of the act Interior had approved standards which actually could lead to degradation of even unpolluted streams. President Kimball of NWF issued a statement which went on to say that "unless the present trend is reversed there is a good probability that the Water Pollution Act will turn out to be nothing more than a license to pollute the pitifully small remnants of pure water in America." Of course the proper test of the adequacy of the standards and treatment of water was whether they led to improvement in the quality of polluted waters and to the protection of unpolluted waters.

Kimball's charges were printed in the Congressional Record by Representative John D. Dingell of Michigan and forced Interior to recognize the excessive leniency by its subordinates in its review of state standards. Interior has decided to require that all state standards submitted for approval must include a statement substantially in accord with the Kimball demands. Secretary Udall made statements apparently requiring designing and locating industrial facilities in such a way as to "minimize" hurtful effects on water quality, not removing them altogether. Thus the no degradation proviso is still not free of ambiguity.

Currently advanced treatment which removes all or nearly all pollutants is still not being pressed by Interior. At a recent pollution abatement conference for Lake Michigan, the states agreed that phosphates should be removed from effluents and this requires some "advanced" treatment. Thus far only five states have adopted acceptable no degradation language. Unless water quality is carefully monitored and unless polluters are required to clean up their effluents according to a specific time table, the standards could turn out to be meaningless.

All of the approved state standards include implementation plans usually providing for a clean up over a 3-7 year period. While Interior appears to have recovered from its embarrassment of failing to comply with its own regulations and now promises to be good, there is an important object lesson here. Federal officials who administer laws often are under pressure from industry and state and local officials who would have them soften the law's requirements. If the officials are agents of private industry in disguise, they are likely to seek an accomodation which not infrequently falls short of the intents of Congress.

The second point is that countervailing pressures from conservationists and the congressional sponsors are necessary if the purposes of legislation are to be realized. It was the protests of these vigilant forces that forced Interior to rethink its position and proceed to serve the public rather than certain private interests. There always remains the possibility that private interests will continue to bend administration of laws to their interests and that a real solution will only come when the public will have to pay for facilities to prevent pollution of our streams and waters.

L.H.N.

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Household Accidental Poisoning

Drugs, home remedies, household substances and little children are part of the contemporary milieu. Part of the job that must be done by health workers, parents and also governmental agencies is to keep the drugs from the little children. Producers and packagers of the offending substances must be closely controlled because theoretically all chemical poisonings are completely preventable and therefore unnecessary. Primum non nocerne was the ancient injunction to physicians. Now modern drugs are so potent as to make the physician on occasion one of the sources of disorders. Similarly household substances and home remedies familiar but deadly are the cause of numerous poisonings annually.

The poison list compiled by the Accident Prevention Branch USPHS[1] of substances most frequently reported by brand names in 1965 reflects the buying habits of housewives and the contents of her bathroom, bedroom and kitchen. The top ten include aspirin, furniture polish, bleach, thyroid tablets and contraceptive pills. We must attribute to the mass communication media serious guilt because they encourage careless handling of dangerous substances. They stress flavor of "baby aspirin" but not the hazard of improper use or storage. They glamorize useless products such as cigarettes and mouth washes. They abet the speed mania by advertising sport model cars bearing wild animal names.

Boric acid is glibly advised for eye wash and eye compresses although quite useless. It possesses no advantage over clean isotonic salt solution. It has been banned from many hospitals as a result of poisonings from ingestion of topical solutions and even from percutaneous absorption. A sizeable portion of fatal cases from salicylate poisoning is caused by methylsalicylate.[2] It is attracted to the young because of its food-like odor. It possesses little therapeutic merit as a liniment. Camphorated oil is another time-honored remedy with little efficiency and high toxicity when ingested or given as a retention enema. The national health would suffer no adverse effect if it is eliminated. This would prevent a number of serious camphor intoxications usually with prolonged and possibly damaging seizures. Ammoniated mercury ointment used for years for pyoderma is more toxic and less effective than antibiotics for topical application. This ointment has been termed the last principal potential cause for acrodynia in the United States.[3]

Packaging or closures that resist the efforts of young children are a fruitful field for development. Already we have promising and inexpensive pharmaceutical vials for solid prescription drugs, strip packaged tablets and capsules for safety in home use. We need package improvement for household substances such as detergents, bleaches, furniture polish, drain cleaners, pesticides and the like which would resist efforts of young children to open them. Of course carelessness of adults who leave the containers open is still a great hazard to the young child. A good closure for containers of liquids of all types is still sorely needed.[4]

Flavored tablets are attractive to children for their candylike apparenance, odor and flavor. Little children also cheerfully ingest dangerous amounts of unflavored aspirin and iron tablets, kerosene, bleach, hormones, tranquilizers and other tastless or even evil tasting tablets. Although there is an advantage in ease of administration in a flavored tablet, we still need package improvements and especially education of parent and child attendants. This would have the desired effect of making parents prime targets for effective safety conscious education.

The iron tablet may be a killer, as little as 1 gram of ferrous sulfate is dangerous to a small child and 2 grams has caused death. They are dispensed in poor containers and in bulk. Such tablets are useful but households must learn to handle them in such a manner as to prevent the numerous serious intoxications. The case fatality rate from iron ingestion is much higher than that for any other of the common poisonings except mineral seal-oil polishes.[4] Fortunately desferoxamine is available for the treatment of iron poisoning and may be life-saving. If tablets were unit packaged and in containers with safety closures, poisoning would be eliminated and parents would be alerted to the dangers of their falling into the hands of the young child.

Aspirin is not a benign substance if carelessly handled. If is the leading cause of accidental poisoning by drugs in this country. In countries like Sweden and Israel it is rarely kept about the house and accordingly poisoning is rare. At present compulsory strip or unit packaging is clearly the best available safety measure to adopt for the 300 mg tablet.

The current recommendation for treatment of poisoning is stomach emptying by emesis as follows:[5] 15-20 ml. syrup ipecac followed by adequate amounts of water (a full stomach is necessary.) This may be repeated once if vomiting does not occur in about thirty minutes. An unsuccessful second dose should be followed promptly by intubation and lavage. Most centers having wide experience with syrup of ipecac have reported almost uniformly good results and very few treatment failures follow the use of such a plan. As a result many believe syrup ipecac be kept for emergency use in all homes having small children.

Kerosene ingestion is common where it is used as a cooking and heating fuel. Many ingestions seem to be related to storage of kerosene, paint-thinner and similar liquids in soft drink bottles. Young children recognize the bottles and ignore the unpleasant taste of the contents while they are drinking. Unless there has been massive ingestion most authorities advise against attempting to empty the stomach because of the danger of inducing more chemical pneumonitis than is already present.

Another major concern is furniture polish containing mineral seal-oil or other low viscosity oil. It is a very effective polishing agent but it is extremely damaging to the lung. The case fatality rate for polish ingestion is very high as compared to that for kerosene and the morbidity rate approaches 100 per cent. We must search for safer agents of equal effectiveness, safer packaging of those that must be used and headline type labelling of these agents stating their dangerous qualities.

Household accidental poisonings can be reduced. The medical profession can play a major role in educating the parent in the hazards, in working for better packaging and eliminating useless household remedies and being ready to treat the poisoning once it has occurred.

L.H.N.

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Graves' Syndrome And LATS (Long Acting Thyroid Stimulator)

Graves' and Basedow independently reported between 1835-1843 an illness characterized by diffuse thyroid enlargement, thyrotoxicosis and exophthalmos. Thyroid stimulating hormone (TSH) arising in the pituitary gland or the hypothalamus is capable of stimulating the thyroid gland to produce thyroid hormone and so it was reasonable to believe that Graves' disease was due to hypersecretion of TSH. If this were true then one should be able to find increased levels of TSH in the blood of patients with this illness. Such increased values have not been found. Furthermore if the pituitary gland were producing TSH in increased amounts, this should be shut off by increased amounts of thyroid extract in the blood as a result of the well-known feed-back mechanisms regulating pituitary hormone production. If it is not the pituitary gland that drives the thyroid to overactivity in Graves' disease then what does do this?

Adams, in 1958[1] described a long acting thyroid stimulator (LATS) a gamma globulin in the blood of patients with hyper thyroidism, which he thought was of pathogenetic importance in Graves' disease. If radioiodine is first administered to euthyroid men, then injection of LATS causes its release from the thyroid gland. The effect is long acting with a peak of 8-16 hours after injection and the constituents released are thyroxin and iodide. The thyroid gland when examined histologically shows the changes characteristic of those found in increased thyroid activity. As one might expect such increased thyroid activity suppresses pituitary formation of TSH. Furthermore if TSH is administered instead of LATS, similar thyroid effects are observed.[2]

Ochi and de Groot[2] report that more than half of serums of patients with hyperthyroidism exhibit LATS activity and this may increase up to 80 per cent when the serums are concentrated. Furthermore the highest figure are especially prevalent among the patients with exophthalmos. The quantity of LATS in the serum correlates well with the size and hyperactivity of the thyroid gland. If prednisone is administered to patients with Graves' disease, it reduces both the activity and the exophthalmos. This raises the suspicion that in some way Graves' disease may be an auto-immune process. The remission induced by prednisone is followed by a rise in serum LATS after withdrawal of the prednisone.

LATS is not found in the pituitary gland of patients with Graves' disease and its level in the serum does not decline after hypophysectomy. What then is it and where does it arise? We get a clue to the answer from MacKenzie's[3] work which showed that lymphocytes from the blood of patients with LATS can synthesize it when the cells are grown in tissue culture. The substance is found to be associated with a gamma globulin fraction of serum protein (IgG) and can be completely or partially neutralized with antibody to IgG.[4] It is therefore itself a gamma globulin.

If LATS is a gamma globulin formed by lymphocytes, then antithyroid drugs should not affect its concentration in the serum. This in fact has been shown by Kriss.[4] Furthermore if the theory enunciated above, that it is an autoantibody to thyroid tissue is true, then LATS should slowly disappear after total thyroidectomy and this is in fact what has been found. The conclusion warranted from such reasoning and experimental verification is that LATS is an antibody against an autoantigen released in response to thyroid injury of some kind.

It is known that Graves' has a high familial incidence. Furthermore men and children rarely suffer from auto-immune diseases. Similarly Graves' disease is more common in adult women than in men and children, and also is characteristically a disorder with cyclic phases of exacerbation and remission. This increases the evidence in favor of Graves' disease being an auto-immune disease. Add to this the fact that several abnormalities of the lymphoid system and putative auto-immune disorders have been associated with Graves': thymus enlargement, lymphocytosis including large lymphocytes, splenomegaly, Hashimoto's thyroiditis, pernicious anemia, rheumatoid arthritis and myasthenia gravis. In addition in Graves' disease antibodies are often found against gastric parietal cell and against intrinsic factor. Finally a lymphocyte cell infiltration in the thyroid gland of Graves' disease is quite similar to that in the autoimmune Hashimoto's thyroiditis. While it is impossible at present to prove absolutely that Graves' dsease is caused by an autoimmune mechanism, there is abundant evidence that abnormalities of immune homeostasis are characteristically associated with this disorder.

What is certain is that a protein with many characteristics of an autoantibody directed against a thyroid antigen is present in the plasma of most patients with Graves' disease and that this LATS is probably the causative factor, stimulating the thyroid to overactivity to produce the Graves' syndrome.

L.H.N.

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Ortho Molecular Psychiatry: I.

The brain provides the molecular environment of the mind which is a synonym for the functioning of the brain. The term orthomolecular is a greek-latin hybrid which expresses the idea of the right molecules in the right amounts. Orthomolecular treatment of mental disease is the attempt to provide the optimum molecular environment for the mind especially the optimum concentration of substances that are normally present in the human body. An example is phenylalanine which is normally present in the brain in small amounts because it contains an enzyme which converts the amino acid to tyrosine. Those children without this enzyme develop higher than normal amounts in the brain and other tissues and this is toxic. We can't restore the enzyme and so the infants are treated by reducing phenylalanine in the diet, there-by saving them from mental retardation.

The function of the brain thus is dependent on its composition and structure that is on the molecular environment of the mind. The presence of LSD, mescaline or some other schizophrenogenic substance produces profound psychic effects. So does No_2 and the phenomenon of general anesthesia, all illustrating the dependence of the mind on its molecular environment.[1]

For the mind to function properly, there is required the presence in the brain of molecules of many different substances as for example those mental diseases associated with physical disease which result from a low concentration in the brain of any one of the following vitamins: thiamine, nicotinic acid or nicotinamide, pyridoxin, cyanocobalamin, (B_{12}) biotin, ascorbic acid, folic acid. There is evidence also that mental function and behavior are also affected by changes in the concentration of the brain of any of a number of other substances that are normally present such as L—glutamic acid, uric acid and gammaamino butyric acid (GABA) and the already mentioned phenylalanine. Out of this has arisen the concept of "optimum molecular concentrations" about which much work has been done in microbiology.

Linus Pauling, the Nobel Laureate in biochemistry points out that the functioning of the brain and nervous tissues is more sensitively dependent on the rate of chemical reactions than the functioning of other tissues and organs. He believes that mental disease is for the most part caused by abnormal reaction rates as determined by genetic constitution and diet and by abnormal molecular concentrations of essential substances. The operation of chance in the selection for the child of half of the complement of the genes of the father and mother leads to bad as well as good genotypes and the selection of foods and (drugs) in a world that is undergoing rapid scientific and technological change may often be far from the best. Significant improvement in the mental health of many persons might be achieved by the provision of the optimum molecular concentration of substances normally present in the human body. Among these substances the essential nutrilites may be the most worthy of extensive research and more thorough clinical trial than they have yet received.

One important example of an essential nutrilite that is required for mental health is vitamin B_{12}. A deficiency can be produced by a genetic defect leading to deficiency of the intrinsic factor—mucoprotein as occurs in pernicious anemia. It can occur in infestation with Diphyllobothrium whose high requirements for B_{12} results in deprivation of the host. Excessive bacterial flora in blind intestinal loops also use up B_{12}. These conditions lead to mental illness often more pronounced than the physical consequences and the mental symptoms are often observed in patients for several years before any physical manifestations of the disease appear. This is especially true of the natural history of pernicious anemia (PA).

A pathologically low concentration of B_{12} in the serum has been reported to occur for a much larger proportion of patients with mental illness than for the general population. Of 396 patients admitted to a Norway mental hospital, the incidence of pathlogically low and subnormal levels of B_{12} in the serums was 15.4 per cent as compared to 0.5 per cent in the general population or 30 times as much. Other investigators have confirmed these findings in Copenhagen[2] and have suggested that B_{12} deficiency, whatever its origin, may lead to mental illness.

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their psychosis as well as of the physical manifestations of this disease and for this purpose only small doses were required. The recommended daily allowance was stated to be 12 mg. per day for a 70 kg. male. Apparently, however, some severe psychiatric distrubances were reported as successfully treated by use of 300 to 1500 mg. per day.[2] In none of these patients were the physical symptoms of pellagra present or any other avitaminosis. Hoffer and Osmond since 1952[3] have advocated and used nicotinic acid in large doses in addition to the conventional therapy for treatment of schizophrenia. Their recommended dosage was very high, 3-18 grams per day per patient as determined by the response of the patient of either nicotinic acid or nicotinamide together with 3 grams of ascorbic acid per day. These drugs are easy to administer, can be taken for years if necessary with only small probability of incidence of unfavorable side effects.

Mental symptoms (depression) are known to accompany the physical symptoms of vitamin C deficiency (scurvy). This vitamin has been used to some extent in the treatment of mental disease and the recommended daily intake is 75 mg. per healthy adults, but it is known that there is a wide variability in the requirements of individual members of a species as much as 20 fold in guinea pigs and probably also humans have a similar large range.[1]

Schizophrenics have a smaller than normal concentration of ascorbic acid in their serum because they have greater power to oxidize N.N.—dimethyl-p-phenylenediamine. This difference has been attributed to the poor diet and increased tendency to chronic infections of the patients. But it has also been interpreted as showing an increased rate of metabolism of ascorbic acid by the patients. Pauling after analyzing the literature is of the opinion that many schizophrenics have an increased metabolism of ascorbic acid presumably of genetic origin. In this case ingestion of massive amounts of ascorbic acid would tend to restore the optimum molecular concentration of ascorbic acid in the brain and have some value in the treatment of mental disease.

Other vitamins (thiamine, pyridoxin, folic acid) minerals such as Zn., Mg., uric acid, tryptophan and glutamic acid influence the functioning of the brain. Pauling reviews the work on glutamic acid. It is present in high concentration in brain and nerve tissue and plays an essential role in the functioning of these tissues. Favorable results for glutamic acid therapy of convulsive disorders have been reported in one out of three patients with petit mal epilepsy. It increased learning ability of white rats and this led to study of the effects of glutamic acid on intelligence and behavior of persons with different degrees and kinds of mental retardation. The effective dosage of glutamic acid is usually between 10-20 grams per day given in three doses with meals and is adjusted to the patients as the amount somewhat less than that required to cause hyperactivity.[5]

Improvement in personality and increase in intelligence by 5-20 I.Q. points has been reported for many patients with mild or moderate mental deficiency by several investigators.[5] It is clear that the function of the brain is affected by the molecular concentration of many substances that are normally present in the brain. The optimum concentration of these substances in the brain may differ from person to person, when one takes into account the concentration provided by his normal diet and genetic machinery.

L.H.N.

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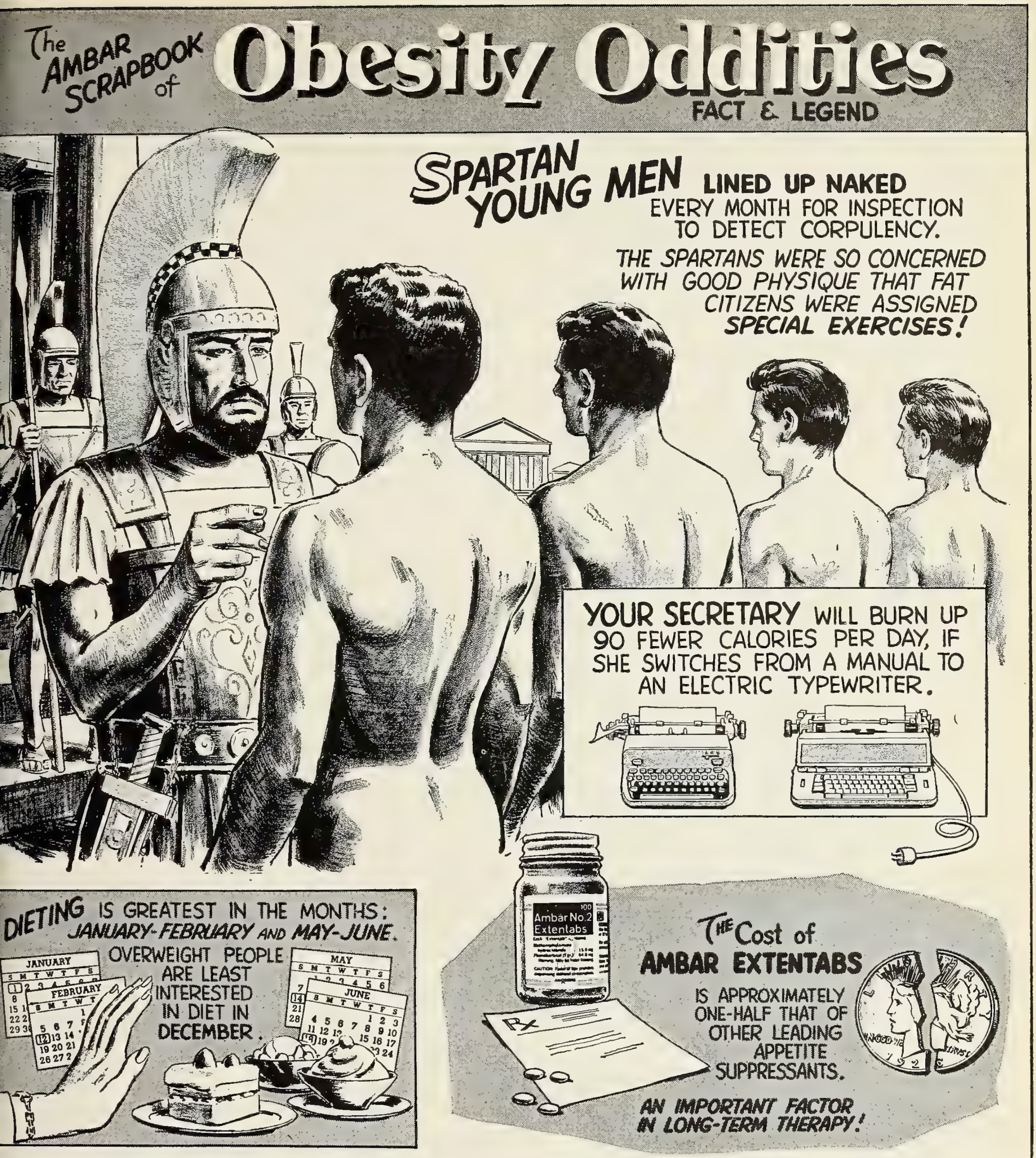
A New Test For Criminal Responsibility

For a hundred years the fixing of responsibility for a crime has depended not so much on the instructions the jury receives as on the jury's sense of what is just and necessary. This is because the issue of criminal responsibility is in large measure a philosophical question of morality and social policy. In these areas the psychiatrist cannot claim any special competence. The elusive concept of "mens rea" loosely translatable as criminal intent does not easily lend itself to any degree of scientific accuracy. Nevertheless it is important to consider when a person can be held responsible and when not responsible for a criminal act.

The American Law Institute has proposed a test for criminal responsibility which has last year been adopted in Massachusetts courts and an increasing number of other states. It states in part "a person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is not responsible for criminal conduct if at the time of such conduct as a result of mental disease or defect he lacks substantial capacity either to appreciate the criminality (wrongfulness) of his conduct or to conform his conduct to the requirements of law."[1] This language replaces the familiar language of the McNaghten test, in which the defendent is exculpated if he did not have the capacity by reason of mental illness or defect to "know the nature and quality of the act or know he was doing what was wrong."

It also replaces the rarely successful "irresistible-impulse" defense which has been the second basis for finding of "not guilty by reason of insanity" in Massachusetts and some other states. This movement for change arose from the objections of some psychiatrists that the McNaghten language was too restrictive and simplistic, that there was rarely if ever an absolute yes or no answer to the "right-wrong" question when it was put to an expert witness. It was further pointed out that the McNaghten test did not allow for a consideration of emotional and other factors in the complicated mental apparatus that influences human behavior and are at least as important as intellectual awareness or cognition.

The irresistible- impulse defense had also been too narrowly interpreted to relate only to sudden spontaneous unconsidered acts and had left out acts following brooding and reflections which could not be exculpated on the grounds of "irresistible-impulse" no matter how overwhelmingly impulsive they were. In the American aw Institute test the objections were largely corrected. The words "substantial capacity" establish that the lack of capacity to appreciate or conform need not be absolute. The word appreciate allows for considerations other than pure cognition. Finally the words "lacks substantial capacity . . . to conform his conduct to the requirements of the law" avoids the implication that criminal acts reflected upon before their commission are automatically excluded.

McGarry[2] points out, however, that for several reasons it is not likely that there will be a significant increase in the number of defendants found not guilty by reason of insanity. One reason is the very restrictive consequences for the defendant that follows such a finding. In Massachusetts if the crime is a homicide, a mental hospital commitment is mandatory during "his natural life."[3] Such a person remains in a quasi-criminal status and his release into the community requires either a Governor's pardon or an order of the Supreme Judicial Court. Except for a capital case there is therefore little advantage to such a plea since the maximum sentence for manslaughter is twenty years with parole eligibility very much sooner.

The second and major reason McGarry gives is that mentally ill persons have infrequently been brought to trial. Many have instead been committed before trial as incompetent to stand trial. As a result the number of defendants found not guilty by reason of insanity amounts to less than a handful each year in Massachusetts. The new test probably will not significantly alter current practices because there will occur the same division of experts at future trials of the issue of criminal responsibility as in the past. In spite of testimony in one case (McHoul) that he was "schizophrenic also had a brain disease" and that he could have been irresistibly impelled, he was found guilty of four counts connected with two attempted rapes and sentenced to an aggregate of 34-45 years.

The new test is encountering the same difficulty as the old because the issue of criminal responsibility although a psychiatric problem, must also include philosophical aspects of morality and social policy. When society catches up in its view of the criminal with enlightened scientific understanding of human psychodynamics then the law will follow and accept the new test for criminal responsibility.

L.H.N.

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Scientists Protest Research On Infectious Diseases As Weapons

A scientific symposium honoring the 25th anniversary of Fort Detrick, the Army's biological warfare research center in Frederick, Maryland, provoked sharp opposition in the biological community and suffered a boycott that is believed to be unparalleled in the recent stormy history of relationships between the military and the scientific community. At least 16 scientists refused to give papers at a Detrick sponsored symposium on nucleic acids as part of a half-spontaneous, half-organized protest on the use of science for destructive purposes. The battle over the symposium generated considerable heat on both sides of the dispute. Pickets marched outside Detrick's main gate carrying signs that proclaimed "Fort Detrick is NOT a

Respectable Scientific Institution" and "Fort Detrick Scientists are Prostitutes." One sign asked "Want to Get Sick? Consult Your Local Physician at Fort Detrick;" and several signs were decorated with drawings of skulls.

Detrick's silver anniversary celebration included two scientific symposiums: one dealing with entry and control of foreign nucleic acids (viruses), the other concerning "leaf abcission April 8-9 (defoliation). Some like Mark Ptashne, a junior fellow at Harvard declined to participate on the grounds that he found Detrick's work "highly repellent" and did "not want my name associated with Fort Detrick." Dean Fraser, professor of microbiology at Indiana University balked at "celebrating the fact. . . It seems at best a little like commemorating the creation of the electric chair and at worst like celebrating the establishment of Dachau" (Hitler's gas chambers).

As the date for the symposium drew near the protest movement against it acquired a semblance of organization. The full extent of the boycott of Detrick may never be known for Detrick has refused to reveal either the names or the total number of scientists who were invited to speak. Nevertheless it is clear the boycott was widespread. Science[1] has been able to identify twenty scientists who declined to give papers. A number of the scientists who were invited to attend the symposum as guests also boycotted, but the extent of this boycott is unknown. Those who did speak at the symposium many of whom were Detrick or former Detrick people were virtually unanimous in proclaiming the program a success.

Those scientists who attended the Detrick conference and the AIBS officials who supported the conference cited a variety of reasons for their actions. One was that the symposiums were unclassified and participation does not imply endorsement of using infectious diseases as weapons. Another reason was that the work was basic, available to all in the open literature anyway, and that a basic researcher can't control applications others might make of their work in weapons development. "Can we place the blame for Hiroshima on Einstein?" Another reason given was that a boycott of the symposiums would merely render Detrick even more secret and defensive. Outside scientists should maintain contact with Detrick in accord with the principle of civilian control of the military. Some of Detrick's work was worthwhile such as the detection of infectious diseases before the onset of symptoms.

Another argument used was that biological weapons are a necessary part of the nation's arsenal, someone has to work on them. Anyhow where does one draw the line. If one boycotts Detrick why not boycott other agencies for war, universities and institutions that perform war work, scientists who hold war grants and so on.

On the other side the boycotters also cited a variety of arguments including the following. Infectious diseases as weapons are immoral, destructive of life and should be opposed by life scientists and physicians who are dedicated to the healing of the sick and the preservation of health. Even if scientists accept the need for biological weapons they should not celebrate the anniversary of an institution such as Detrick which is devoted to destructive purposes. Furthermore participation by outside scientists in Detrick activities provides an aura of respectability for work devoted to perfecting the horror of infectious diseases as weapons.[2]

Another argument of the boycotters was that participants who discuss their work at a Detrick conference may directly contribute to development of biological weapons. Detrick scientists profit more from a meeting where they can question scientists and learn of work in progress than they would by waiting for results to be published.

The boycott was surprising to almost everyone involved. The army and the AIBS had not anticipated such sharp opposition to the program. Most of the protesters had not anticipated that such a sizable number of their colleagues would refuse to speak. Without doubt the episode reflects a new mood of our nation. Many are becoming tired of warfare in Vietnam and in the cities. But whatever the underlying cause of the protest, it provides an intriguing glimpse into the dynamics of a moral crusade. It gives us a view into the ways in which moral feelings are awakened.

Psychologists such as Kenneth Keniston[3] who are interested in exploring the psychodynamics of the development of the moral trait in young people will find in this story a fertile field for further study.

L.H.N.

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Correcting Hyperlipemia

The pathological deposition of cholesterol containing placques in the intima of the aorta and other large arteries is the characteristic lesion of atherosclerosis. The mechanism of this deposition is uncertain but concomitant changes in the composition of the blood have established that an association between elevated plasma levels of cholesterol and triglycerides and atherosclerosis does exist. Accordingly efforts have been directed towards reduction of blood cholesterol in the hope that this would lessen the degree of vascular cholesterol deposits. These attempts have utilized a variety of methods both dietary and pharmacologic.

The physician must first determine whether the patient's hyperlipemia is primary or secondary to some other disease such as diabetes or hypothyroidism. Secondary hyperlipemia can usually be corrected by adequate treatment of the causative disease. When the hyperlipemia is primary and the principle abnormality is hypercholesterolemia, fat restriction and substitution of polyunsaturated for saturated fat is usually an excellent and effective dietary change. If hypertriglyceridemia is the chief lipid abnormality or both triglyceride and cholesterol concentrations are elevated dietary carbohydrate restriction is usually very effective. Ideally one would prefer to control biochemical abnormalities by means of diet, but many patients are either unable or unwilling to adhere to a diet. Even with excellent patient cooperation the resultant biochemical alterations are often inadequate and the profession has searched for pharmacologic agents that could correct the hyperlipemia.

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The ideal hypolipidemic agent would be one which effectively lowers serum lipids and lipoproteins, is non toxic, is easily administered and is free from annoying side effects to the patient. The compound which most closely approximates these criteria is a-p chlorphenoxyisobutyrate (CPIB—Astromid S, Clofibrate). Initially it was believed that clofibrate acted best with androsterone but Hellman[1] demonstrated in 1962 that clofibrate alone possessed all the hypocholesterolemic and hypotriglyceridemic and other properties ascribed to the combination of clofibrate and androsterone.

The primary effect of clofibrate is to reduce plasma concentrations to triglyceride-rich lipoproteins of low density and also low density cholesterol rich lipoproteins to a lesser degree. This results in a reduction of plasma triglyceride levels averaging 30-40 per cent of cholesterol levels averaging 15-25 per cent. In addition lipoprotein lipase activity appears to increase so that the height and duration of post-prandial lipemia is decreased.[2]

Clofibrate also has a salutary effect on clotting by reducing fibrinogen levels reducing platelet stickiness which is important in preventing the white thrombus of arteries. It prolongs platelet survival, reduces clot lysis time and prevents the shortening of recalcified clotting time which occurs during post-prandial lipemia.[3] There are other effects mostly minor and no evidence of toxicity in animals or man. It reduces blood uric acid levels mostly in patients with elevated triglyceride and uric acid levels.[4] Most patients achieve a satisfactory result without a change of diet. One difficulty is that for some unknown reason about 15 per cent of the patients show no response to clofibrate administration.

The precise mechanism of action is presently speculative. However, it does not depend for its action on the thyroid or adrenal, and it inhibits cholesterol synthesis not late in the cholesterol biosynthetic cycle but at the beginning by inhibiting acetate incorporation into cholesterol. This is an ideal site of inhibition of cholesterol synthesis whereas those drugs that acted late in the cycle like Mer 29 led to an accumulation of desmosterol, a toxic agent producing serious side effects. This agent is virtually free of side effects, has no known toxicity and there are no known contraindications except that patients on anti-coagulant drugs may require less dosage when they also receive clofibrate.

The dosage is generally 3-4 half-gram capsules a day depending on body weight. This dosage results in a sustained lowering of plasma lipids and lipoproteins for as long as four years. Associated with the fall in plasma lipids is visible regression of deposits of tissue lipids such as zanthomata and lipemic evidence in the retina of diabetic patients.[5] One may assume that there is also regression of lipid deposits in the intima of the coronary and other arteries although no direct proof exists. This is a crucial question which it is hoped will be answered by the many cooperative studies with clofibrate that are under way in this country and Britain. The next five years should provide firm answers as to whether reduction of plasma lipids will favorably influence the incidence of infarction, reinfarction or death in patients with ischemic heart disease.

A small percentage of patients, however, do not respond to clofibrate, so that it is not always possible to predict the individual's response. Other drugs such as nicotinic acid and cholestyramine may reduce hypercholesterolemia that is not affected by clofibrate. Furthermore, the physician should be aware that a decrease in serum cholesterol concentrations may not occur for many months after the start of treatment with clofibrate.

A decision to treat involves several practical considerations. One is to recognize that there are normally occurring fluctuations by as much as 30 per cent and so it seems reasonable to base decisions about treatment on the degree and constancy of abnormalities over a period of months. Another related problem is the specific level at which treatment should be begun. The philosophy, however, is that primary prevention and the corrections of abnormalities before they cause overt disease is the ideal to which we must strive.

Because cardiovascular disease is the leading cause of death in the U.S. all patients who present for a periodic examination should have determinations of serum cholesterol, triglycerides and at least a single post-challenge blood glucose examination. For the cooperative patient early detection and correction of conditions that increase risk of CHD are the most promising approach to prevention.

L.H.N.

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THERAPY OF REFRACTORY IDIOPATHIC THROMBOCYTOPENIC PURPURA[1]

Milton Cooper, M.D.,[2] Robert S. Briggs, M.D.[3] and Stuart C. Finch, M.D.[4]

There is general agreement that corticosteroids and splenectomy represent the two major modes of treatment of patients with idiopathic thrombocytopenic purpura (ITP), but the indications for their application are controversial. The approach we have followed in adults for acute ITP is intermediate between those who advocate early splenectomy and those who rarely splenectomize but rely almost solely on corticosteroids for maintenance of remission. Initial therapy consists of strict bed rest and the immediate institution of from 80 to 100 mg of prednisone daily. Usually tissue bleeding will greatly diminish or stop within 24 hours following the initiation of prednisone therapy. If the platelet count returns to normal, the prednisone is slowly tapered during the next 4 to 6 weeks. If there is failure to respond to corticosteroids within two weeks, splenectomy is performed. If thrombocytopenia recurs concomitant with or following steroid withdrawal, the full dose of corticosteroid is restored and splenectomy is performed after the platelet count has reached the range of 100,000/mm^3 or greater. The approach in children usually is more conservative since viral infection is frequently responsible and steroid induced permanent remissions are common. Sometimes the children receive several courses of prednisone before a permanent remission develops. Rarely do we employ platelet transfusions in our patients with ITP since the survival of the platelets in these patients is extremely short. For patients with intractable bleeding despite adequate corticosteroid therapy, however, transfusion with fresh donor blood prior to emergency splenectomy may be necessary in order to reduce bleeding during surgery. Fortunately, these situations are rare since emergency splenectomy under these circumstances carries a high mortality.

In our experience, the platelet counts of 75-80% of adults with ITP will either substantially increase or completely recover in response to the initial course of corticosteroid. Most, however, relapse when the corticosteroid is reduced and will eventually come to splenectomy. About 70% of those splenectomized will respond with complete remission of long or permanent duration. Some patients, however, will respond well for a few days or even a few weeks following splenectomy and then will relapse. Patients who respond to the initial course of corticosteroid are more likely to achieve a good result from splenectomy than those in whom corticosteroid has little or no effect.

Patients who either fail to respond or relapse following splenectomy constitute a major problem. Their clinical courses and responses to other forms of treatment are most unpredictable. Platelet counts tend to fluctuate making therapeutic evaluation most difficult. Some patients will not bleed with platelet counts of 10,000/mm^3 or less while others will bleed with platelet counts in the range of 30,000/mm^3. The course usually is chronic and many of the patients are quite incapacitated by this disability. It is the management of this group with chronic refractory ITP that we wish to devote this discussion. The following cases have been chosen for presentation, both to illustrate, 1) the variety of therapeautic approaches that have been utilized in intractable cases and 2) that these therapeutic approaches are virtually the same despite the differences in disease etiology.

Case 1). The patient was an 11 year old female who was hospitalized at St. Vincent's Hospital in Bridgeport in October of 1963 with ecchymoses and petechiae, one month after a respiratory infection. Examination was essentially negative except for the presence of scattered petechiae and ecchymoses.

Laboratory studies revealed: hemoglobin 12.5 gm%, hematocrit 35%, WBC 6,900/mm^3 with normal differential. The platelets were 10,000/mm^3. A direct Coombs test was positive. Lupus tests were negative. The bone marrow was hyperplastic, and the megakaryocytes did not appear to be producing platelets. There was increased marrow eosinophilia.

The Hospital course was complicated by epistaxes with the hemoglobin falling to 6 gm%. She was given fresh blood.

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This research was supported by Public Health Service Research Grants HE-08493-04, *and* 5-M01-00038-03, *and Public Health Service Training Grant* HE-5316-05.

Prednisone therapy was instituted at 60 mg. per day, without effect upon the platelet count. She was discharged on prednisone, 45 mg. per day. During the next several months there was no platelet response to this dose of steroid, but she did develop a marked Cushingoid appearance.

In December of 1963, 50 mg. and later, 100 mg. of 6-mercaptopurine were given on a daily basis. Hemoglobin levels, which had been averaging 9 to 10 gm%, rose to 12 gm% and in the subsequent month, platelets rose to 90,000/mm^3 while the prednisone was gradually reduced to 20 mg. per day. The improvement was of short duration, however, and by February 1, 1964, the platelet count again had dropped to critical levels. The hemoglobin and hematocrit values remained normal. 6-mercaptopurine was stopped and on February 16, 1964 a splenectomy was performed. The platelet count rose to 335,000/mm^3 on the third post operative day, but then rapidly returned to low levels despite maintenance of prednisone. In the subsequent weeks she had much difficulty with oral lesions, skin lesions and epistaxes.

In late March 1964, she was admitted to Yale-New Haven Hospital. Initial laboratory reports were as follows: hemoglobin 8.4 gm%, hematocrit 25%, WBC 29,300/mm^3 with 71% polymorphonculear cells. Platelet count was 12,500/mm^3 and the Coombs test was positive.

From April 2, 1964 to April 9, 1964 she was fed 1 liter per day of an uncooked homogenate of calf spleen without significant improvement. On April 10, 1964, this was increased to 2 liters per day following which there was steady improvement in her level of circulating platelets. At the time of her discharge on April 24 her platelet count was 136,000/mm^3 and her hemoglobin was 12.1 gm.%. From that time to the present, the patient's platelets have remained normal or slightly elevated.

Comment: This combination of ITP and Coombs positive acquired hemolytic anemia are the features of the Evans syndrome. The serious problems in management of this disorder are well illustrated in this patient. The relationship between the poor platelet response to the initial course of corticosteroid and the relatively poor response to splenectomy was experienced. The apparent response to bovine spleen homogenates has been observed by us in one other patient of a group of 6 (4 of whom are included in this paper).

Case 2). This 30 year old female was first seen and admitted to St. Vincent's Hospital, Bridgeport in October 1959. She reported that she had always tended to bruise easily, but this had been increasing during the previous 6 months and was associated with menorrhagia. The only other significant history was an episode of arthritis and arthralgia about 4 or 5 years prior to admission. The positive physical findings essentially consisted of obesity and diffuse petechiae and ecchymoses.

Significant laboratory studies included: hemoglobin 8.8 gm% hematocrit 24%, bilirubin, total 3 mg.%, indirect 2.5 mg.%, platelets 40,000/mm^3, reticuloycte count 15.3%, Coombs positive and Lupus tests negative. Marrow studies revealed normoblastic hyperplasia and megakaryocytes with poor platelet formation.

The patient was diagnosed as having an Evans syndrome and was treated with corticosteroids. There was an excellent remission. However, as the steroids were tapered, the hemoglobin and platelet levels gradually fell, with a marked exacerbation of her bleeding. She was readmitted to the hospital in March of 1960. At this time, in addition to the laboratory and clinical evidence of marked thrombocytopenia and hemolytic anemia, she had developed splenomegaly. Following transfusions a splenectomy was performed in March of 1960 (Yale-New Haven Hospital).

The platelets gradually rose post-operatively, and at the time of discharge were 100,000/mm^3. She continued to do well on gradually decreasing doses of steroids, and in June 1960 the platelets were 300,000/mm^3 and the hemoglobin was 12 gm.%. However, as the daily dose of prednisone was dropped to 10 mg., the hemolytic anemia clinically exacerbated. This was controlled by increasing the steroids to 30 mg/day. Subsequent to October 1960, though the hemolytic anemia was never a serious problem, the thrombocytopenia remained, despite varying doses of steroids. Menorrhagia was the most marked clinical problem, and neither it nor the osteoporosis that developed (nor, incidentally, the thrombopenia) were affected by large doses or premarin and progesterone.

In 1963 she was placed on 600 mg hydroxychloroquine sulfate per day for a period of 2 months without improvement in the blood picture.

In June 1964 she was admitted to Yale-New-Haven Hospital where lupus preparations again were found to be positive. She was fed 2 liters of calf spleen per day for two weeks without improvement. On her way home from New Haven, she developed abdominal pain and was readmitted to St. Vincent's Hospital. Within twenty-four to thirty-six hours after the onset of pain, her situation had so deteriorated that surgery appeared impossible.

Laboratory studies were reported as follows: hemoglobin 12 gm.%, hematocrit 37%, WBC 83,550/mm^3 with 83% polymorphonuclear leukocytes. Her platelets were 30,000/mm^3. Lupus tests were positive. Blood urea nitrogen was 31 mg.%. She died on July 4, 1964. Autopsy revealed a thrombosis of the superior mesenteric artery with small bowel infarction. There were no diagnostic changes in the superior mesenteric artery, nor in any other organ but the kidney. Here, however, were found changes consistent with lupus.

Comment: This patient had disseminated lupus erythematosus with an Evans syndrome. Despite persistent thrombocytopenia and bleeding that were resistant to several forms of therapy, it is ironic to note her death was secondary to thrombosis. Actually, this phenomena is not unheard of in lupus erythematosus, but the possibility that it occured in response to the administration of calf spleen has been seriously considered.

Case 3). This patient was first seen in July 1959 at the age of 35, having been referred to St. Vincent's Hospital for splenectomy for ITP following several months of unsuccessful corticosteroid therapy.

Examination revealed a moderately obese, mildly Cushingoid female. Other than ecchymoses and petechiae, the only positive findings were a scar and irradiation changes over the lower abdomen, (the result of therapy for a sarcomatous uterine lesion treated at age 18).

Laboratory studies were within the normal range except for thrombocytopenia. Lupus and Coombs tests were negative.

Splenectomy was performed, with a post-operative rise of platelets to 120,000/mm^3, then a return to pre-operative levels. This unresponsive state persisted despite corticosteroid therapy until October 1959, when on 40 mg. of prednisone per day the platelets started to rise and remained at levels over 100,000/mm^3 despite reduction in prednisone to 10 mg per day.

In February 1960 she relapsed again, and no further remission ever was obtained even with increase of steroids to 100 mg. per day. In March 1960, she was seen at the New England Medical Center where an attempt was made to suppress the immune process with thioguanine. Platelets only decreased to new lows. In January 1961, she developed signs and symptoms of chloecystitis and cholelithiasis, and coincident with this, an increase of platelets to adequate levels. A chloecystectomy was accomplished without incident. Thrombocytopenia occurred promptly in the post-operative period.

During the next few years, multiple forms of therapy were instituted. In 1963, she was given hydroxychloraquine sulfate for three months. In 1964, she received a homogenate of bovine spleen for two weeks, and in 1965, 6-mercaptopurine for a few months. None of these therapeutic modalities changed the platelet count.

In April 1966, she was readmitted to the Hospital with a history of a few months of generalized aches and pains. A survey shortly before admission revealed a mild anemia, markedly elevated sedimentation rate, and a normal platelet count. It was felt that this might be a phase of previously undiagnosed lupus. However, just prior to the hospitalization, the patient developed rectal bleeding. Proctoscopy revealed a carcinoma, approximately at the level of bowel fixation, probably related to her previous surgery and irradiation. There was evidence of metastases, and, in view of her symptoms, 5-fluorouracil was administered.

Over the next four to five months, her platelets remained at relatively adequate levels except when affected by 5-fluorouracil. There was no generalized bleeding, but there was some local bleeding due to the necrotizing carcinomatous lesion.

She was admitted for the last time in August of 1966, following an episode of bleeding which seemed to subside. However, without further apparent blood loss, she became vague and disoriented, appeared to slip gradually, and died several days following admission. Despite early refrigeration, she became bloated post mortem, and it was quite evident she had an agonal clostridia infection.

Case 4). This 45 year old patient was first seen in April of 1963. She reported fairly frequent epistaxes and increased bruisability since childhood. Menarche had been at age 13, and menses had always been prolonged. Tooth extractions had been performed without difficulty. Thrombocytopenia was first diagnosed in 1960. Splenectomy was performed in 1960 with only transitory improvement. Menorrhaghia persisted and became so severe that in 1962, a radium insertion was performed. She was referred because of persistent epistaxes, bruises and petechiae.

Examination was negative, except for the splenectomy scar, numerous petechiae and ecchymoses, and chronic pigmentous changes of the legs.

Initial laboratory tests revealed a normal hemogram. Platelets were 38,000/mm^3. Marrow revealed hyperplasia with no significant platelet formation from megakaryocytes. Lupus clot tests were persistently negative. No other serologic abnormalities were detected.

In the subsequent years, she had numerous hospital admissions to St. Vincent's Hospital in Bridgeport, the New England Medical Center in Boston, and Mt. Sinai Hospital in New York. Multiple therapeutic regimens were attempted and all were ineffective. Prednisone, in varying doses, controlled bleeding, but took its toll in problems related to osteoporosis and edema. Anabolic therapy only increased edema. 6-chloropurine, chlorambucil, hydroxychloraquine sulfate, and 6-mercaptopurine were administered without improvement. She was also fed 1500 g. daily of beef spleen for two weeks at the Yale-New Haven Hospital without effect.

She was hospitalized in 1964 for compression fractures, in May 1966 for edema (following prolonged use of an anabolic agent) and a painful, swollen left buttock lesion (treated with depomedral), and in October 1966 for intractable epistaxes.

In early March, she was given I.V. methotrexate which only brought platelets to a new low. Shortly thereafter, the persistent enlargement of her left buttock and hip increased in size, became "hot" and was associated with high fever. Coincident with this event, the patient's platelets rose to 100,000/mm^3 and persisted at this level. An initial incision and drainage released huge amounts of purulent material containing an anaerobic streptococcus and proteus vulgaris. However, the fever persisted, and multiple antibiotics were ineffective. A wider incision was made permitting greater drainage, the fever gradually subsided, and so did the level of this patient's platelets.

Comment: Cases 3 and 4 also failed to repond to multiple modalities of therapy. In both, the only increase in platelets was associated with extensive necrotizing lesions. Such observation might suggest another therapeutic approach. However, in contrast, one often sees the patient who has done well following steroids and splenectomy, suddenly relapse with the development of either severe infection or trauma.

Discussion

Idiopathic thrombocytopenic purpura appears to result principally from the accelerated destruction of circulating platelets, probably through the action of platelet antibodies or other anti-platelet factors. Anti-megakaryocytic factors, however, also may play a role through their adverse effects on platelet production. The disorder may arise acutely with sudden onset of bleeding manifestations, or it may be of gradual onset and extended duration.

The clinical manifestations of thrombocytopenia, identical to that termed "idiopathic" may occur following a viral illness, with infectious mononucleosis, with or following the administration of some drugs, in association with a collagen disease (particularly lupus erythematosus), or together with a lymphoproliferative disorder. Not infrequently, it it difficult to differentiate from thrombotic thrombocytopenic purpura. Thrombocytopenia also may result from generalized impairment of hemopoiesis (most notably toxic, nutritional, myelophythisic, or idiopathic aplastic) and from accelerated sequestration and/or destruction of the circulating cellular elements of the blood by the enlarged spleen of another disease, viz, hypersplenism. Physical abnormalities and history will often separate these kinds of thrombocytopenia from the idiopathic variety. In any event, the differentiation frequently can be made through study of the peripheral blood and bone marrow since the white and red cells frequently will be affected by the same process. Tests for lupus factor and heterophile antibody also may help to establish the proper diagnosis.

The bone marrow picture in idiopathic thrombocytopenic pupura is not diagnostic. Erythroid and myeloid elements usually are normal, but megakaryocytes frequently are moderately increased in number. Sometimes there is a modest eosinophilia. Although the somewhat immature megakaryocyte with reduced platelet budding is frequently present in idiopathic thrombocytopenic purpura, it is not characteristic. A bone marrow examination is performed, therefore not so much to make the diagnosis of idiopathic thrombocytopenic purpura, as to exclude other disorders which may produce thombocytopenia.

Although the prognosis of patients with chronic refractory idiopathic thrombocytopenic purpura remains poor, the situation now is not hopeless. Following splenectomy the platelet counts in some patients may be reduced, but are high enough to prevent serious spontaneous bleeding. Some patients with more severe thrombocytopenia will maintain platelet levels high enough to prevent bleeding with small maintenance doses of prednisone. The problems associated with long term administration of corticosteroids are formidable, however. Transfusion of viable platelets does not constitute a valuable form of treatment of chronic ITP. Circulating anti-platelet factors will greatly accelerate the sequestration and destruction of the transfused platelets. Furthermore, repeated administration of platelets will foster the development of platelet isoantibody which will further shorten the survival of transfused platelets.

Recent medical reports indicate that 50% or more of all patients with chronic refractory ITP will respond to immunosuppressive therapy (1-4). Our limited results have been less impressive, however, and in some patients we have failed to observe a sustained response after some initial success despite continuation of immunosuppressive therapy. Most experience has been gained with the drug 6-azathiaprine, a closely related analog of 6-mercaptopurine. This drug may be administered for months in moderate doses without significant hematologic depression, but other complications may develop. Immunosuppression also has been achieved with 6-mercaptopurine, methotrexate, thioguanine and 6-chloropurine. Despite lack of complete success with this group of drugs, the future for this form of therapy looks bright—especially with the development of various forms of combination immunosuppressive therapy.

The rationale for trials with antimalarial drugs (hydroxychloroquine) is based on the lupus erythematosus etiology of thrombocytopenia of many patients. Only four patients have been studied to date, but none has responded. One other patient has been treated with both penicillamine and BAL without evidence of any platelet response. The hope in this instance was to interfere with antibody complexes that might be coating and injuring platelets.

Monto et al. reported recovery from chronic ITP in a single patient given large amounts of raw calf spleen by naso-gastric tube[5]. We now have administered 1 liter of raw calf spleen by mouth for a minimum of 2 weeks to 6 patients with chronic refractory ITP. During therapy the platelet counts of 2 patients returned to normal and the patients have had no recurrence in over 3 years. One other patient (Case 2) developed a fatal mesenteric thrombosis at the end of the treatment period despite persistent thrombocytopenia. At the moment there is no reasonable explanation for these favorable responses. They may have been coincidental, but the observations deserve further exploration.

Finally, mention should be made of the striking increases in circulating platelet levels which develop in some patients with tumors or infections or following trauma. One might suggest that tissue degradation products either stimulate platelet production or interfere with their accelerated destruction but certainly the actual mechanisms involved are quite unknown. Demonstration and isolation of a platelet stimulating component in human tissue is an interesting therapeutic challenge.

Summary

A variety of therapeutic modalities now are available for patients with chronic idiopathic thrombocytopenic purpura who have failed to respond to either corticosteroids or splenectomy. Transient re-

sponses to either inflammatory or neoplastic disease and permanent responses concomitant with raw bovine spleen administration have been noted. Our limited experience with immunosuppressive agents and antimalarial compounds has been quite disappointing. Evaluation of the results of various forms of therapy in chronic idiopathic thrombocytopenic purpura is difficult because of the high frequency of spontaneous remissions and exacerbations.

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MEDICINE IN THE NATION

I was elected president of the Association for the year 1923-1924, and so was offered a unique opportunity for helping to bring Western medical activities forward and to get better coordination in all parts of the country. Indeed, I consider my presidency of the American Medical Association about the most important experience of my medical career. It brought me wide contacts in the field of medicine and a responsible opportunity to view what could be done through the national organization in advancing research and medical education. Always my effort in the organizational side of medicine was to further advances in medical research in the care of the patient and its public health and social relationships. Apparently a rather general feeling was that a good deal was to be done about the medical curriculum, about better social relationships, and about a better coordination between East and West. With the advance of scientific medicine so many problems and pressures were presenting themselves, some of them seeming nore pressing at the time to the physician, that perhaps it is not to be wondered at that progress in the field of the social relationships of medicine was to be such a long, slow pull.—Robinson, E. E., and Edward, P. C. (eds.): *The Memoirs of Ray Lyman Wilbur 1875-1949,* Stanford, Calif: Stanford University Press, 1960, pp 302-303.

EVALUATION OF PURPURA IN WOMEN

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The problem of understanding purpura in women, like the general problem of understanding women, often is a riddle with an enigma. Purpura of some degree in otherwise healthy women is so common that it rather infrequently is brought to the attention of a physician. When severe, prolonged, cosmetically unattractive or thought to be dangerous, the patient may confront her doctor with purpura as a chief complaint. Some of these patients have obvious disease that is easily demonstrated (although not so easily treated) and we will not dwell on these at any length. Others have rare or exotic underlying diseases that require a rather sophisticated workup. Finally, some patients have problems so bizarre that they defy the most careful diagnostic investigations and force us into areas of inadequate medical knowledge where we can only speculate on the pathophysiology of the purpura.

The chronic appearance of purpuric spots on the lower extremities of otherwise healthy women usually is not due to serious disease. It is essential, however, to completely investigate the bleeding and coagulation mechanisms at least once on each patient with recurrent purpura before identifying it as one of the benign disorders. A careful medical history and physical examination often will lead to a close approximation of the correct diagnosis. Each patient then should have a bleeding time by the Ivy method, a prothrombin time, a partial thromboplastin time, examination of the stained blood smear, and an accurate enumeration of the platelets by a phase microscopy technique.[1]

The combination of normal coagulation tests, negative family history and absence of other bleeding, points toward a benign form of local purpura. Most of the sporadic purpura of the legs of women is of this type. The range in frequency and severity of these lesions is wide and their occurrence in large numbers sometimes is alarming. A single cause usually is not apparent, but the principal factors are unrecognized trauma, poor tissue tone, and increased vascular fragility, sometimes constitutional or familial in type. During the premenstrual period these patients frequently experience increased numbers of purpuric spots. Patients with diabetes and hypertension tend to have increased vascular fragility which predisposes them to the development of purpura. Some women with a variety of skin diseases may develop a recurrent extensive purpuric or petechial eruption that is most disfiguring and include such disorders as Schamberg's disease, Majocchi disease, angioma serpiginosum and the Ehlers-Danlos syndrome[2]. During the later years of life, loss of vascular supporting structures along with vascular degeneration permit the development of "senile" purpuric spots. Although the lesions often occur on the legs they are more frequently observed on the forearms and hands. They usually present as flat, sharply demarcated, single or confluent, non-tender, red or deep red spots. Senile purpura is disfiguring and sometimes frightening, but it is not dangerous. On the other hand, it must be differentiated from the more serious forms of purpura caused by amyloid infiltration of blood vessel walls, paraprotein coating of platelets, or hyperglobulinemia due to a variety of causes. Purpura simplex and the simple easy bruising known as "devil's pinches" have been seen in almost all women at some time in their menstrual life (usually with a menstrual irregularity). They are mild and more significant from the cosmetic standpoint than from that of physical disability.

Psychogenic purpura is a vague entity includes some deeply religious individuals in a state of ecstasy and some plain psychoneurotic women with a poor adjustment to life.[3] They may have ecchymoses on the palms of the hands and dorsum of the feet or on the forehead, sometimes with the configuration of the crucifix. These patients often go from doctor to doctor seeking some sort of salvation when they might really benefit more from a religious counsellor or a psychiatrist.

A most interesting type of purpura is the autoerythrocyte sensitization syndrome which was first described by Gardner and Diamond in 1955.[4] Although it is extremely rare, we recently reported 3 cases[5] which brought the total reported in the world literature to 26. The syndrome probably is more common than these figures indicate, however, as Creger[6] has recently reviewed the subject and mentioned that he personally has observed 6 unreported cases, and knows of several others. The reported

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cases have all been women ranging in age from 17 to 64 years, most of them with rather profound emotional problems. The lesion is characterized by a "stinging" or other premonitory sensation in the area before the onset of purpura. At first there is a bright red, erythematous patch, followed in a few hours by a bluish discoloration at the edges of the reddened area. The lesions are painful, and after 12 hours resemble a bruise except for unusual edema, heat and pain. The lesion may be reproduced and the diagnosis established by injecting intradermally 0.1 ml of an 80% suspension of washed autologus or compatible isologous erythrocytes, or erythrocyte stroma. One of our cases was unique in that she also responded reproducibly to phosphatidyl serine extracted from either erythrocyte stroma or mammalian brain. The significance of this is not at all clear, but we suggested that a form of local allergic vasculitis may develop secondary to the extravasation of erythrocytes and the breakdown of their membranes with release of substances "foreign" to the local tissues against which there is a reaction. Creger has speculated that the syndrome may represent the absence of an inhibitor of bradykinin, but he has published no evidence in support of this.

Closely related to the autoerythrocyte sensitization syndrome is a deoxyribonucleic acid (DNA) sensitivity syndrome. There have been 3 separate reports[7,8,9] of women with repeated attacks of painful, swollen, reddish, then ecchymotic lesions of the arms and legs. These patients then demonstrated an extraordinary reaction to DNA and lysed leukocytes, but not to RNA, packed erythrocytes or erythrocyte stroma. One woman had an exquisite reactivity to histamine[10] but not to other test materials. The explanation of these unusual and bizarre syndromes remains speculative. Some authors believe that the autoerythrocyte and DNA type purpuras are primarily psychogenic in origin.[11] Although emotional factors probably play a significant role in the evolution of the syndrome, it seems likely that altered skin reactivity contributes more directly to formation of the actual lesions.

Purpura factitia consists of lesions deliberately induced by self-flagellation or sucking or other injury to the skin. They are usually located on the arms or legs or anterior trunk but never on the back. Often they are in lines. Even when finally and irrefutably observed inducing the lesion, the patient will rarely admit that she has inflicted it upon herself and will usually "play dumb."[12,13,14] Sometimes these cases are extraordinarily difficult to differentiate from other forms of purpura restricted to women and one has to go through an exhaustive workup to rule out such conditions as psychogenic purpura or autoerythrocyte sensitization. Sometimes pending litigation for compensation plays an important role.

Case #1—In August of 1965 this 26 year old married female dropped a bottle on the floor of a supermarket resulting in widespread glass dispersion. The glass particles allegedly struck her lower legs and ankles producing several small lacerations. She stated that she was able to remove several glass fragments from the left leg during the next few days. In January of 1966 she recalled that several pieces of glass emerged from the skin of both legs. Subsequently she has occasionally found glass fragments on the skin of other body areas. In March of 1966 she first developed a few non-painful spontaneous purpuric spots on her lower extremities. Usually these lesions were small but recurred in crops. Sometimes they were associated with a "pinching" sensation at their onset, but the lesions were never hot or swollen. At about the same time that she first developed purpura she noted small red spots on her chest and abdomen. She consulted a physician who performed X-ray studies of the legs. These were negative. She then consulted a surgeon concerning the possibility of having glass particles excised from her leg. He found no indication for surgery. Soon thereafter, she noted occasional purpuric spots on her arms.

The past history revealed that the patient had been moderately obese for years and had been unable to lose weight. She was troubled with occasional migraine headaches and dysmenorrhea. The family history was unremarkable.

The physical examination showed a moderately obese, intelligent white female with a single 3 cm. ecchymosis on the lateral aspect of the left leg. A few cherry angiomata were present on the chest. Otherwise the physical findings were unremarkable.

Hematocrit, leukocyte count, differential leukocyte count, platelet count, bleeding time, prothrombin time and partial thromboplastin time all were normal. Skin tests with her own red cells and DNA were negative.

Comment: This attractive, but moderately obese married female had no hemorrhagic diathesis or evidence of residual tissue damage from her previous trauma. She seemed bored with her existence and preoccupied with the idea that circulating glass particles were responsible for her troubles. She now has instigated legal proceedings against the store where her injury was incurred. There was no evidence that the purpura and petechiae were factitious or of the autoerythrocyte type, but there was little evidence that they were of organic origin.

Case #2—In December of 1965 this 48 year old, single white female was admitted to the Yale-New Haven Hospital for investigation of her purpura. She was well until 1953 when she first noted the onset of recurrent purpuric lesions on her arms, head, trunk and legs. These usually were of spontaneous origin and frequently were preceded by local pain about 24 hours earlier, and sometimes by fever. Skin lesions often developed at the spot where someone had touched her.

During the next ten years she continued with recurrent crops of purpura at intervals of every 3-4 weeks. She also developed episodes of severe right frontal headaches which often lasted from 1 to 7 days. There was a rare fainting spell. She also noted that her skin became quite sensitive so that heavy clothes bothered her a great deal. Generalized weakness and progressive weight loss developed. She had worked as a school secretary, but had been unable to work since 1963 because of her illness.

There was no history of epistaxis, menorrhagia or melena. Her only operations consisted of an appendectomy in 1948, several tooth extractions in 1950 and splenectomy in 1958. None of the surgery was associated with excessive bleeding. Her system review revealed that she occasionally had slight ankle edema, but no cardiac symptoms. Her appetite had remained excellent, but her weight had fallen from 124 lbs. to 84 lbs. during her 12 years of illness. Her menstrual periods were regular but were accompanied by severe dysmenorrhea which had necessitated hormone therapy. At times she had experienced vague pains in her legs, but no joint symptoms. The family history revealed that her father had died at age 77 of heart trouble. Her mother was living and well, but had had a breast cancer removed 11 years previously. Her fiance died of a brain tumor about 5 years prior to the onset of her illness.

During the 12 years of her illness she consulted many physicians and several hematologists. Numerous bleeding and coagulation tests were performed, but all were negative. Corticosteroids and antibiotics were tried without success. The reason for the splenectomy was unclear since the lowest platelet count ever recorded was 130,000/mm^3. She was moderately improved for about 6 months following splenectomy. During the few years just prior to admission she began taking several Demerol tablets daily for her headches.

The physical examination revealed a thin, somewhat hirsutic lady with a flat affect. She was pleasant and intelligent. There was a moderately course tremor of the hands. Several recent purpuric spots were present on the legs, but none were noted elsewhere on her body. There was 1+ bilateral ankle edema. A Grade II systolic murmur heard best along the left sternal border and over the pulmonic area was noted. The remainder of the physical examination was negative.

Laboratory studies showed an hematocrit of 44% with 3% reticulocytes. The platelet count was 560,000/mm^3. The white count was 8,450/mm^3 with a differential of 39% segmented neutrophils, 6% band forms, 1% eosinophils, 38% lymphocytes and 16% monocytes. The BUN was 8 mg % and the PBI was 7.0 μg%. Total protein was 6.3 gms% with an albumin of 3.8 gm% and normal electrophoretic patterns. urinalysis was unremarkable. Skin testing of the forearms with autologous erythrocytes, saline, erythrocyte lipid, phosphosphatidyl serine, DNA and RNA all were negative.

The patient refused psychiatric consultation. She was returned to the care of her private physician with several therapeutic suggestions.

Comment: This patient represents a rather severe form of psychogenic purpura with some of the classical features of the autoerythrocyte sensitization syndrome. However, she did not demonstrate hypersensitivity to her own red cells, and at the present time, by definition, this or a similar demonstrable sensitivity is an essential feature of this syndrome. The characteristic features of the psychogenic purpura which she demonstrated are the pain preceding local lesions, the persistence of pain at the site of the purpura, the location of the lesions, and the recurrance of the lesions in "crops". Also consistent with this diagnosis are the histories of a deceased fiance several years before onset, fatigue and malaise, headaches and dysmenorrhea.

Allergic (sometimes called anaphylactoid) purpuras are of about equal frequency in males and females. Purpura may develop as a single episode with acute onset or it may have frequent remissions and exacerbations over a period of months or years. Often there may be other symptoms of allergy such as urticaria, erythema or serous effusions. Most patients with this disorder are asymptomatic, but some may have joint symptoms of the type described by Schölein in 1837[15] or gastrointestinal symptoms of the type described by Henoch in 1874.[16] Not infrequently, patients with allergic purpura will develop glomerulonephritis.[17] Those with gastrointestinal symptoms may go on to intussusception or perforation.[18] The etiology of this disorder may be foods,[19] drugs[20,21] or even bacterial infection, but in at least half the patients no definite etiologic agent can be identified.[22,23,24]

Coagulation factor deficiencies usually present as hemophilia or hemophilia-like syndromes, but patients with mild forms of these disorders may bruise easily. Almost invariably, however, there is abnormal bleeding with surgery or dental extractions, and laboratory studies may demonstrate abnormalities of either the prothrombin time or partial thromboplastin time.

Although clotting factor deficiency disorders are generally more common in men, one entity, frequently observed in women should be mentioned. It is von Willebrand's Disease.[25] This disorder may be the most common form of coagulation disorder in women and not infrequently the diagnosis is missed. It is transmitted as an autosomal dominant trait. The usual history is that of a lifetime of easy bruising and excessive bleeding with minor cuts or surgery. Some patients experience massive bleeding with surgery. Almost invariably the clotting time, prothrombin time and prothrombin consumption are normal. The partial thromboplastin time usually is normal or borderline. The bleeding time, however, almost invariably, will be prolonged if carefully performed by the Ivy technique and a moderate to fairly severe reduction in plasma levels of factor VIII (anti-hemophilic globulin) will be detected by special assay methods. Sometimes even these studies will be within normal limits and in these instances it probably is justifiable to diagnose von Willebrand's Disease on the basis of history alone. Certainly, it should be prepared for if surgery is contemplated.

Another coagulation problem somewhat peculiar to women is that of chronic coumarin ingestion. This problem is particularly common in nurses and para-medical personnel who have access to a variety of coumarin-type anticoagulants. Strong suspicion of this entity should be aroused in any woman with purpura and bleeding associated with a prolonged prothrombin time.

A rather ill-defined and quite rare group of disorders is associated with quantitatively normal numbers of platelets which are either anatomically, physiologically or biochemically abnormal. These have been variously called qualitative platelet defects, thrombasthenia, thrombocytopathia and have eponyms associated with the names of Glanzmann, Naegeli, Fonio, Jurgens, but have not been clearly characterized.[26] Qualitatively abnormal platelets are occasionally found in uremia and acyanotic heart disease. That they are functionally abnormal is sometimes demonstrable by using the patient's platelets in the thromboplastin generation test with normal serum and absorbed plasma. Their abnormal nature may also be demonstrated by electron microscopic examination, or by enzyme assays. Some of the patients have very prolonged bleeding times.

A quantitative increase in platelets is called thrombocythemia and may be associated with purpura in some cases of chronic myelogenous leukemia, polycythemia vera, myeloid metaplasia, disseminated cancer, or essential thrombocythemia. The platelets perform perfectly well *in vitro* if diluted down to the normal range, but their increased numbers *in vivo* can lead to either thrombosis or hemorrhage with purpura.

If the platelet count is below 100,000/mm^3 the bleeding probably is due to thrombocytopenia and it then is essential to perform a bone marrow aspiration. The presence of normal or increased numbers of megakaryocytes is compatible with increased peripheral destruction or utilization of platelets. This may be due to underlying vasculitis, hypersplenism, diffuse intravascular coagulation, intercurrent viral or bacterial infection, drug sensitivity[27] or antibody[28] that either directly or indirectly destroys platelets. In many instances, however, there is no apparent cause for the thrombocytopenia and the disorder must be considered either the acute or chronic form of idiopathic thrombocytopenic purpura. This type of thrombocytopenia is fairly common in women and has been described in depth in a number of excellent reviews[29,30,31] and standard texts.[32,33]

Thrombocytopenia associated with reduced or absent bone marrow megakaryocytes usually indicates bone marrow injury due to physical agents or drugs resulting in inadequate delivery of platelets to the peripheral blood. This may occur in individuals who are either inordinately sensitive to, or have been exposed to excessive quantities of these exogenous factors. Pharmacologic depression of marrow function is becoming an increasingly common problem in both sexes, but is seen more frequently in women, probably because they take more drugs. In some women, however, reduced megakaryocytic activity may be secondary to severe bone marrow disease such as leukemia, metastatic cancer, multiple myeloma, uremia, megaloblastic or aplastic anemia.

Summary

Purpura is a common disorder in women. Frequently it is of benign origin. Sometimes it is life threatening or fatal. It may run the gamut from an obvious drug induced thrombocytopenic purpura to a bizarre psychophysiologic reaction whose pathogenesis remains obscure. Its differential diagnosis and management are always a challenge to the skill and perspicacity of the clinical hematologist.

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TEACHING AND THINKING

'Tis no idle challenge which we physicians throw out to the world when we claim that our mission is of the highest and of the noblest kind, not alone in curing disease but in educating the people in the laws of health, and in preventing the spread of plagues and pestilences; nor can it be gain-said that of late years our record as a body has been more encouraging in its practical results than those of the other learned professions. Not that we all live up to the highest ideals, far from it—we are only men. But we have ideals, which mean much, and they are realizable, which means more. Of course there are Gehazis among us who serve for shekels, whose ears hear only the lowing of the oxen and the jingling of the guineas, but there are exceptions. The rank and file labour earnestly for your good, and self-sacrificing devotion to your interests animates our best work.—Osler, W.: *Aequanimitas,* ed 3, New York: McGraw-Hill Book Co., Inc., n.d., p. 119.

SOME ENZYME CHANGES OF CLINICAL IMPORTANCE IN LEUKEMIA

Leonard S. Kaplow, M.D., Stuart C. Finch, M.D., and Joseph R. Bertino, M.D.

In a review of leukemic leukocyte metabolism, Valentine[1] writes, "The application of enzymatic and biochemical technics to the problem of leukemia rests squarely on the assumption that abnormalities in cell growth, differentiation and behavior should be mirrored in altered cell metabolism". One might assume that the detection of such abnormalities would require highly sophisticated technics. For some intracellular biological substances, this is indeed so. However, simple procedures are also available, which not only detect altered cell metabolism but may, in addition, provide the clinician with practical data, permitting more accurate diagnoses and more effective treatment.

The present report briefly discusses three leukocyte enzymes of significance in leukemia, which have either diagnostic or therapeutic value. The first, alkaline phosphatase is an intracellular cytoplasmic enzyme, which may be easily assayed cytochemically and which is helpful in leukemia diagnosis. The second is lysozyme* (muramidase). This enzyme is released from degraded leukocytes and appears in plasma, where it may be readily measured. The extracellular concentration of this enzyme is particularly helpful in the classification and diagnosis of leukemia. Dihydrofolic acid reductase, the third leukocyte enzyme to be discussed, has important therapeutic implications.

Leukocyte Alkaline Phosphatase

The presence of alkaline phosphatase activity in leukocytes was first indicated by Kay[2] in 1929. It is only in the last decade, however, that clinicians, especially hematologists, have been excited by reports concerning changes in the activity of this intracellular enzyme system in a variety of physiologic and pathologic conditions.

Alkaline phosphatase, one of a large group of hydrolytic phosphomonoesterases, can be readily assayed biochemically and easily demonstrated histochemically. One of us[3] has described a staining technic for demonstrating peripheral blood leukocyte alkaline phosphatase (LAP). The method is dependent on the ability of the enzyme to cleave phosphate from naphthol phosphate esters. The liberated naphthol is bound to a diazonium salt present in the incubation mixture to form an insoluble colored azo dye at the theoretical sites of enzyme activity. When used in conjunction with a "scoring" method, based on the intensity of staining of one hundred neutrophils, a numerical representation of LAP activity can be obtained. The range of scores varies from zero to a maximum of 400. Normally, adult human LAP is found in the cytoplasm only of occasional segmented neutrophils and scores range from 10 to 100, with a mean of 60. In many stressful situations, however, LAP activity increases markedly (Figure 1). During pregnancy and in the newborn period, activity is five times normal, or greater. Elevated values have also been consistently found in most patients with bacterial but not viral infections.

One of the most interesting findings in reference

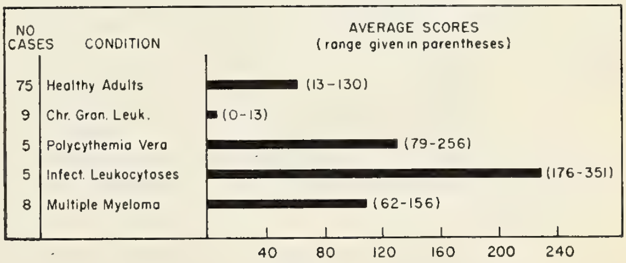

FIGURE I

Leukocyte alkaline phosphatase activity (Azo dye cytochemical scoring technique) in health and in various disease states.

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* The officially designated name for this enzyme now is muramidase, but the more commonly used term 'lysozyme' is used in this paper.

to LAP has been the great reduction in activity seen in the leukocytes of almost all untreated patients with typical chronic myelogenous leukemia (CML). This is in marked contrast to patients with leukemoid reactions or with myelosclerosis with myeloid metaplasia where elevated LAP activity is usually seen and where depressed levels are almost never encountered. In patients with CML, scores tend to return to normal with remissions and frequently rise above normal during terminal blastic crises. The associated finding of deletion of a portion of the number 21 (Ph^1 or Philadelphia) chromosome in CML has prompted speculation that the gene controlling leukocyte alkaline phosphates is located on the deleted portion of this chromosome. Additional suggestive evidence of this has come from the observation that in Down's syndrome, in which there is trisomy of the number 21 chromosome, LAP scores average one-third above normal. However, there is strong evidence against such a hypothesis and the control, function and significance of LAP remains poorly understood. Hormonal regulation has been suggested, and adrenocortical steroids and estrogens have been reported as influencing LAP levels. Activity is independent of serum levels of alkaline phosphatase and unrelated to sedimentation rate or plasma proteins. Although activity frequently is increased in conditions accompanied by a leukocytosis, normal or low LAP scores are not uncommonly found in association with markedly elevated white blood cell counts.

Increased LAP activity is also seen in most patients with polycythemia vera, lymphoma, multiple myeloma and Hodgkin's disease. Significantly, normal values are usual in secondary erythremic states. Following therapy, LAP scores often drop to normal levels in Hodgkin's disease and this has been interpreted by some as a favorable prognostic sign.

Other diseases characterized by low or absent LAP are hereditary hypophosphatasia, paroxysmal nocturnal hemoglobinuria and sideroblastic refractory anemia.

Perhaps most stimulating to investigators in the field of hematological cytochemistry, is the knowledge that mature cells which look identical when stained with the usual polychrome (Wright's, Giemsa) stain, may differ markedly in biochemical make-up. This is well exemplified on blood smears stained for LAP activity, where two adjacent cells may show widely differing activities (Figure 2). Whether these findings are due to differences in the chronological or physiological age of such cells remain unanswered.

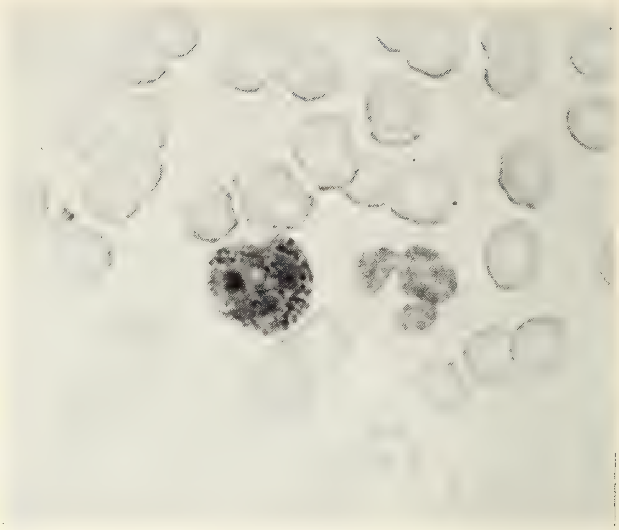

FIGURE II

Blood smear stained for leukocyte alkaline phosphatase activity showing variation in intensity of staining of neutrophilic granulocytes.

Assessment of LAP activity is a simple and rapid staining procedure which is now of proven usefulness in the diagnosis of a variety of disease states and which offers another parameter for assessing the effects of stress on human physiology. The reader is referred to a recent review article[4] for a more detailed description of this fascinating enzyme system.

Lysozyme

Lysozyme was accidentally discovered in 1922 by Sir Alexander Fleming while searching for a universal antibiotic.[5] He was most excited about this new finding, and made many fundamental and important observations concerning its physical characteristics and biological distribution. Soon he realized, however, that the antibacterial spectrum for lysozyme was too limited to be of great clinical value. His subsequent search for a more potent antibiotic eventually led him to the discovery of penicillin. Recently there has been a resurgence of interest in this enzyme because of its possible applications in the field of hematology.

Lysozyme is present in fairly high concentrations in mature granulocytes and monocytes in all stages of development.[6] There is now good evidence that the measurable lysozyme in serum is derived mostly from the degradation of these cells.[7] Consequently, one would expect high concentrations of this enzyme in the serum of patients with either monocytic or granulocytic leukemia, where the mass of these cells is markedly increased. Normal or low levels should be present in the serum of patients with lymphocytic forms of leukemia. The situation is comparable to the release of transaminase from the increased breakdown of liver cells in hepatitis. The results of recent studies at Yale, in patients with acute and chronic leukemia, have confirmed these expectations[8] (Figure 3). Most patients with monocytic leukemia have extremely high serum lysozyme levels, with the average value higher than 100 μg/ml (normal 7-14 μg/ml). In acute and chronic granulocytic leukemia, serum lysozyme levels, although elevated, are generally not as high as they are with monocytic disease. Normal or subnormal levels are found in patients with either acute or chronic lymphocytic disease. These findings have been of great value to us in acute leukemia classification. In a few instances, morphologic classification of acute leukemia type has been changed because of the results of the enzyme studies.

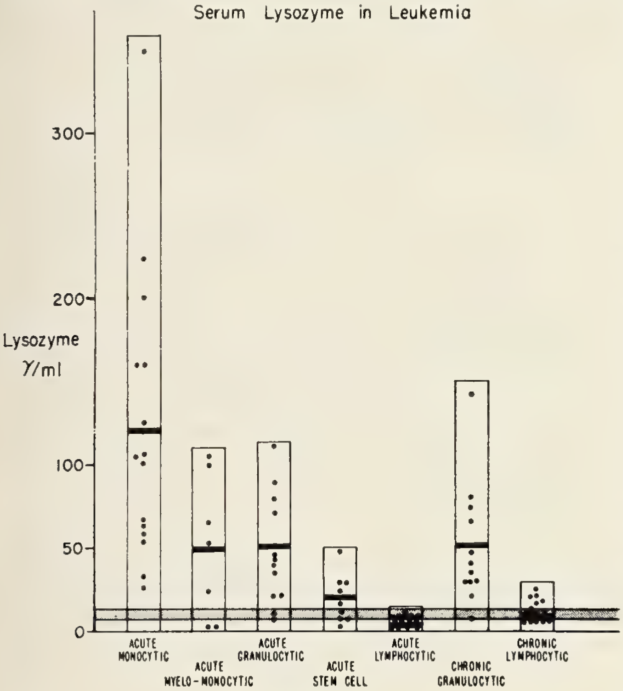

FIGURE III

The cross-hatched long horizontal bar represents the normal range of serum lysozyme activity. The short, solid horizontal lines within each vertical column represent average serum lysozyme activities in each leukemic group.

Lysozymuria does not occur in healthy subjects and its detection suggests granulocytic or monocytic leukemia, renal disease or sarcoidosis.[9,10] Some patients with monocytic leukemia may excrete several grams of this enzyme daily. Serum lysozyme levels over 50 μg/ml usually are associated with lysozymuria.[9]

It is our belief that serum and urine lysozyme studies are not only helpful but may be essential for the proper evaluation of the acute leukemias. Whenever there is the combination of a greatly increased serum level of lysozyme and lysozymuria, the patient probably has acute monocytic or myelomonocytic leukemia. A normal or low serum level associated with a blastic leukocytosis almost invariably indicates acute lymphocytic or stem cell leukemia.

We strongly urge wider use of this test, which is simple and easily within the grasp of virtually all clinical laboratories.[11]

Dihydrofolate Reductase

The third enzyme, dihydrofolate reductase, as mentioned previously, is more difficult to assay, and its estimation has heretofore been restricted to research laboratories. Although not of value from a diagnostic viewpoint, it is valuable in testing and developing new folate antagonists[12] and may eventually provide the clinician with a guide for evaluating folate antagonist (e.g., Methotrexate) therapy. This essential enzyme, necessary for the conversion of the vitamin, folic acid to its coenzyme form, tetrahydrofolate, subsequently functions as a one carbon donor for several important synthetic reactions, in particular purines and thymidylate the pyrimidine unique to DNA. Table I is a summary of the activities of this enzyme measured in normal peripheral blood, bone marrow and leukemic leukocytes. It may be seen that this enzyme is not unique to leukemic leukocytes, but rather is associated with cell immaturity. Not known is why this enzyme actively decreases with differentiation of both leukocytes and erythrocytes.

The significance of this enzyme lies in its susceptibility to inhibition by the folate antagonists, amethopterin and aminopterin. Thus, complete

TABLE I
LEVEL OF DIHYDROFOLATE REDUCTASE IN LEUKOCYTES

Source	*No. Subjects*	*Enzyme Activity umoles/hr/mg*
Normal Leukocytes	15	0.001 (0-.001) *
Bone Marrow**	4	0.080 (0.06-0.11)
Chronic Lymphatic Leukemia	8	0.001 (0-0.002)
Chronic Myelocytic Leukemia	10	0.040 (0.01-0.09)
Acute Leukemia	22	0.031 (0.01-0.09)

* Range.

** Specimens obtained after lysis of contaminating erythrocytes; approximately 50 per cent immature cells.

inhibition of this enzyme activity *in vivo* by Methotrexate can be correlated with subsequent inhibition of cell replication. It has been possible to monitor intracellular enzyme inhibition in leukemic leukocytes when patients are given Methotrexate, thus providing a method whereby biochemical resistance to this drug may be detected in patients.[12] It may be possible to adapt this test to a histochemical procedure; if successful, this technic could become a useful routine procedure.

Three leukocyte enzymes of diverse function have been briefly discussed from the standpoint of their significance in the diagnosis and treatment of leukemia. They represent only a fraction of the many enzyme systems participating in intracellular biochemical reactions. Nevertheless, as a result of these and other similar studies, one can conclude that variations in leukocyte enzyme activities may be due to intrinsic differences inherent in particular cell types, or to differences in the chronological or physiological age of cells of similar type, or may result from abnormal metabolic states, as exemplified by leukemia.

Blood is a tissue which may be readily and repeatedly biopsied. Alterations in intracellular enzyme activity detected in a small volume of blood may not only represent changes in the total circulating cell mass but may also reflect physiological abnormalities of the organism as a whole.

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Few people are capable of expressing with equanimity opinions which differ from the prejudices of their social environment. Most people are even incapable of forming such opinions.—Albert Einstein

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X-RAY THERAPY IN THE TREATMENT OF CARDIAC TAMPONADE IN CHRONIC MYELOCYTIC LEUKEMIA.

REPORT OF A CASE

Harvey W. Kaetz, M.D. and Leonard M. Selsky, M.D.

In leukemia, pericarditis as a terminal event or as an autopsy finding is not uncommon.[1,2] However, actual disturbance of cardiac function due to pericardial effusion and cardiac tamponade is rare.[3] When tamponade is present, its recognition and treatment are of vital importance and may tide the patient over until anti-leukemic therapy has an effect. To our knowledge, the case now reported is the first in which roentgen therapy was used successfully in this situation.

F. D. F. (YNHH # B8-68-02) was a 28 year old white truck driver who was admitted to Yale New Haven Hospital on February 22, 1966. He had enjoyed good health until September of 1965 when he noted spontaneous bruising on his trunk and extremities. In January 1966, his physician made the diagnosis of chronic myelocytic leukemia after a blood study. Busulfan, 6 mgm. per day, was given and maintained for three weeks. His status continued to deteriorate, however and therapy was stopped. On admission, the patient was extremely cyanotic, dyspneic, and orthopneic. The neck veins were markedly distended in the sitting position; there was large ascites, massive edema of the thighs, legs and feet, and huge hepato-splenomegaly. Pulsus paradoxicus was noted to be present with unobtainable pulse and blood pressure on inspiration. Fluoroscopy showed no cardiac pulsations, and the chest xray demonstrated the characteristic cardiac enlargement of a large pericardial effusion. Echo cardiography confirmed the diagnosis.

Admission blood studies showed a hematocrit of 33 per cent, (3 per cent buffy coat), a reticulocyte count of 11.4 per cent, a white blood cell count of 155,500 per cu. mm. The differential count on the peripheral blood smear showed 32 per cent mature granulocytes, 37 per cent band forms, 5 per cent metamyelocytes, 18 per cent myelocytes, 2 per cent promyelocytes, 2 per cent monocytes, and 4 per cent lymphocytes. There was marked polychromatophilia and a rare nucleated red blood cell was seen. The platelet count was 1.7 million per cu. mm. All tests for evaluation of blood coagulation were within normal limits. An electrocardiogram showed sino-auricular tachycardia with low voltage in all leads. A pericardial tap was performed via the subxiphoid route and 700 ml of bloody fluid with a hematocrit of 17% was removed. Dyspnea was lessened immediately and the paradoxical pulse disappeared. Post tap venous pressure was 170 mm. of saline. A catheter was placed in the superior vena cava via the right basilic vein to monitor venous pressure. Busulfan was restarted in a dose of 8 mgm. per day. The day after admission (February 23), the venous pressure began to rise and the paradoxical pulse returned. On February 23, the venous pressure was 220 mm. of saline; on February 24, the venous pressure was 240 mm. of saline. This evidence for reaccumulation of pericardial fluid prompted us to try x-ray therapy to the precordium as a rapid, direct & effective way to treat the presumed leukemic infiltration of the pericardium. The pericardial area was treated with 100 r of x-ray on February 24th & 25th. On this latter date, the venous pressure had risen to 290 mm. of saline and 500 c.c. of bloody fluid was removed from the pericardial space. At the end of this procedure, the venous pressure was 110 mm. of saline and a pericardial rub was heard. The pericardial region again was treated with 150 r of x-ray on Feb. 26th & 28th to bring the total therapy to 500 r. On March 2, the venous pressure was 150 mm. of saline; there was no dyspnea. On that date an electrocardiogram showed normal voltage in all leads and the chest x-ray showed a normal cardiac silhouette. At the time of discharge from the hospital on March 9, the liver and spleen were much smaller; the white blood cell count was 23,300 per cu. mm.; the platelet count was 1.6 million per cu. mm. The pericardial rub became inaudible three weeks after hospital discharge. He remained in complete remission until early December 1966 when he developed an acute myeloblastic crisis. He was unresponsive to further medication and died on December 20, 1966.

Discussion

Cardiac tamponade in leukemia is usually unrecognized during life or is noted only in the terminal phase of the disease.[2] In those few cases[2,4,5] recognized during the course of the leukemia, the pericardial effusion did not require removal but responded to treatment of congestive heart failure,[2 4], or was unrelated to the leukemia[5] and required no treatment. It is the authors' contention that this complication may be more frequent than the literature would indicate. Dyspnea, orthopnea, cough, and cervical venous engorgement may point to heart failure in any patient. This is particularly so if there is anemia with cardiac dilatation as may occur in leukemia. But, if there is no anemia and there has been no prior history of heart disease or failure, the sudden appearance of cardiac decompensation should alert the physician to the

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possibility of pericardial effusion and cardiac tamponade.

X-ray therapy to the anterior mediastinum for leukemic infiltration of the heart or its coverings rarely has been used. Blotner and Sosman[6] reported the use of deep x-ray therapy over the heart in a patient with leukemia who had heart block. Temporary disappearance of the block occurred. Cardiac irradiation was tried also in a three year old child[7] with acute leukemia and intractable heart failure with relief of the failure. The case reported herein appears to be the only instance in the literature in which x-ray therapy was used to prevent the reaccumulation of pericardial fluid due to presumed leukemic infiltration of the pericardium.

Summary

A case of cardiac tamponade in a 28 year old white male with chronic myelocytic leukemia is reported. X-ray and other therapy are discussed. The need for awareness of this complication also is emphasized.

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Leaders worthy of the name . . . contribute to the continuing definition and articulation of the most cherished values of our society. They offer in short moral leadership.

The thing that makes a number of individuals a society rather than a population or a crowd is the presence of shared attitudes, habits and values, a shared conception of the enterprise of which they are all a part, shared views of why it is worthwhile for the enterprise to continue and flourish. Leaders can help to bring that about. In fact it is required that they do so. When leaders lose their credibility or their moral authority then the society begins to disintegrate.

Leaders have a significant role in creating the state of mind that is the society . . . They can conceive and articulate goals that lift people out of their petty preoccupations, carry them above conflicts that tear a society apart, and unite them in the pursuit of objectives worthy of their best efforts.—John Gardner. Annual report of the Carnegie Corporation for 1965.

Management of Advanced Lymphoma

Rose J. Papac, M.D.*

In the management of patients of advanced lymphoma, an important distinction exists between the overall care of the patient and the use of specific measures to control the disease. In a patient of this type, in whom long term control of the disease is unlikely, the best clinical judgment is required to decide whether specific therapy can offer worthwhile palliation or whether, indeed, it is wiser to withhold such treatment. Nevertheless, of all the neoplastic diseases the lymphomas are among the most amenable to radiation therapy and chemotherapy.

The decision to pursue specific therapy in patients with advanced lymphomatous disease is dependent upon a number of factors, among which are: the age and sex of the patient, the general condition of the patient, the histologic characteristics of the lymphoma, its anatomic distribution, and the response elicited by earlier treatment. In younger individuals every possible attempt with conventional and investigative forms of treatment is reasonable. Younger age groups tend to respond better than older in the treatment of lymphoma. If, however, the general condition of elderly patients has not deteriorated markedly, trial with conventional forms of chemotherapy is indicated for disseminated forms of lymphoma. The sex of the patient also has a bearing on prognostic considerations. Females have a better prognosis than males.[1-3] This is an age-dependent difference in Hodgkin's disease, however, with survival having an inverse relationship to age in the female (< age 35, 77% 5-year survival; age 55 and over, 36.7%).[2] In the male, age has no prognostic relationship to survival.

When the histologic character of the lymphoma is Hodgkin's disease (of lymphocytic-histiocytic types or nodular sclerosis) or lymphosarcoma of a lymphocytic or Burkitt type, specific therapy is employed with greater enthusiasm than when reticulum cell sarcoma or Hodgkin's of the fibrotic or reticular type is present. The cell type has been shown to be related to prognosis as well as response to treatment.[4] The most favorable group histologically shows lymphocytic lymphosarcoma or Burkitt type lymphoma and Hodgkin's disease as described above.[4-6] While giant follicular lymphoma connotes longer survival when the diagnosis is established, its prognosis when the disease is disseminated is that of the predominant cell type.

Lymphomatous disease which is generalized but confined to peripheral node areas and extra-nodal solitary parenchymal disease are more favorable conditions than intra-abdominal adenopathy, parenchymal invasion with extensive nodal involvement, and generalized disease associated with CNS, bone, liver and lung invasion.[6] The response to prior treatment also is related to probability of improvement with subsequent therapy, and indeed, with survival. While there are relatively few long term studies with the use of alkylating agents, our study as well as a recent report, demonstrate the difference in survival between responders and nonresponders to alkylating agents.[7-8]

In patients who are elderly, cachectic, who have bone marrow failure, and the lymphopenic phase of Hodgkin's disease, it is unlikely that benefit from specific forms of chemotherapy will occur. The best management of such cases consists in measures directed toward control of complicating conditions such as infection, fever, pruritis, anemia, bleeding tendencies, pyrexia, pain, hypogammaglobulinemia and hyperuricemia if present.

The specific measures used in management of disseminated lymphomatous disease include radiation therapy and chemotherapy. Radiotherapy as a form of palliation is most useful for localized areas of symptomatic involvement, particularly when there are spinal cord compression, isolated cranial nerve palsies, lymphomatous deposits in bone, breast, testis, thyroid, isolated portions of the gastrointestinal tract, or unilateral renal involvement. When there is massive splenomegaly, which is symptomatic or associated with the hypersplenic syndrome, radiation therapy to the spleen also provides useful treatment.

Renewed interest has arisen recently in the use of total body irradiation for far advanced lymphoma in cases refractory to all other therapeutic modalities. The results obtained suggest that this still be considered an investigative rather than conventional form of management, since there have been relatively few patients who have been included in the recent studies (Johnson, 6 cases; Jacobs, 15

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Supported in part by the United States Public Health Service Grant No. HE 5316-07

cases).[9-10] The duration of response has been generally brief, although Johnson had 3 impressive remissions of 9, 12 and 16 months.

The types of chemotherapeutic agents with demonstrable effectiveness in the treatment of malignant lymphoma are the alkylating agents, vinca rosea alkaloids, methyl hydrazine, corticosteroids, and some antibiotics, namely actinomycin D and streptonigrin.

Alkylating Agents

The present area of chemotherapy of neoplastic diseases was initiated with the use of nitrogen mustard, an alkylating agent, in the treatment of a patient with lymphosarcoma at Yale-New Haven Hospital in the early nineteen-forties. Since the introduction of nitrogen mustard, hundreds of alkylating agents have been synthesized in an attempt to reduce toxicity and to improve the therapeutic result. Significant biologic differences exist among agents but the therapeutic spectrum of disease responsive to them is in general remarkably similar.[11] A common assumption, although erroneous, is the concept that refractoriness to one alkylating agent confers resistance to the entire group. In our own experience, as well as that of others, a considerable number of patients respond to treatment with a different type of alkylating agent when refractorines to one type develops.[7,12-13]

The predominant toxicity of the alkylating agents is hemoatopoietic, with differences in the character and duration of effect depending upon the particular agent used. Myleran, in therapeutic doses, induces significant granulocytopenia and thrombocytopenia. Lymphopenia is the earliest and most remarkable effect of nitrogen mustard, chlorambucil and cytoxan. Cytoxan has relatively less tendency to cause thrombocytopenia. Hemolytic anemia may reult from the ue of melphalan.

The intravenous alkylating agents induce rapid therapeutic effect, and they are desirable forms of treatment when there is rapid progression of disease, compression of the superior vena cava, the spinal cord or the ureter, pyrexia due to the disease and generalized pruritis. In most other situations, patient can be managed satisfactorily with the oral agents, since these do not have the untoward gastrointestinal effects of nausea and vomiting associated with their use.

When intravenous alkylating agents are given initially, oral agents are generally instituted when marrow recovery following the intravenous agent is evident, usually in two to six weeks. Permanent marrow hypoplasia may result if the oral drugs are initiated earlier, since the regenerating marrow may be more susceptible than normal marrow to the effects of these agents.

The median duration of remission following intravenous nitrogen mustard in Hodgkin's disease is 12 weeks; with subsequent chlorambucil the medium duration is 32 weeks, and with oral cytoxan the median is 30 weeks.[7,14] In lymphosarcoma the response rate is lower, and the duration of reponse to nitrogen mustard is 8 weeks; with chlorambucil or cytoxan the median duration is 20 weeks.[7]

In 1957, aklaloids extracted from the Madagascar periwinkle (vinca rosea Linn) were discovered to have marrow-depressing properties. Subsequent investigation revealed anti-tumor effect in animal systems and in human neoplastic diseases. The greatest clinical usefulness of vincaleukoblastine (Velban) is in the management of Hodgkin's disease.[16] Remissions occur less frequently in patients with lymphosarcoma and reticulum cell sarcoma.

The toxicity of the vinca rosea alkaloids is neurologic as well as hematopoietic, with loss of deep tendon reflexes, paresthesias, occasional obstipation, rarely central nervous system toxicity.

In comparison to the alkylating agents, the response rate elicited with Velban is identical in nonrandomized studies.[13,17-18] In another report velban was found on comparison with cytoxan to be superior, although in this study the dose of cytoxan used was considerably below that what has been considered optimal by other investigators.[17,19-20]

In some centers Velban is, however, regarded as the initial agent of choice in the treatment of disseminated Hodgkin's disease. Because it has neurotoxicity as well as hematologic toxicity, and because it has not shown clearcut therapeutic superiority, we have preferred alkylating agents as the initial drugs in the management of disseminated Hodgkin's disease. While the response rates may be very nearly equal, the median duration of remission with Velban is somewhat less than that of oral alkylating agents—13.3 to 28 weeks, as opposed to 32 or 30 weeks with chlorambucil and cytoxan.[7,16,21]

A cogener of Velban, vincristine, has had clinical trial since 1962, and has also demonstrated tumor regression in patients with Hodgkin's and the lymphosarcomas and the reticulum cell sarcomas.[22-24] There appears to be no cross resistance between Velban and vincristine, although both are stathmokinetic agents. Neurotoxicity is also a prominent side effect of vincristine.

In 1963, the investigation of a group of hydrazine compounds revealed tumor inhibitory effects due to methyl hydrazine (1-methyl-2-benzyl-hydrazine.[25] This compound, whose mechanism of action has been compared to the indirect effects of ionizing radiation has, on clinical trial, its greatest effect in the management of disseminated Hodgkin's disease although other lymphomas have on occasion responded as well.[13,26-27] In Hodgkin's disease the response rate is equivalent to that obtained with the alkylating agents and Velban. A study from the Christie Hospital revealed a remission rate of 15 of 24 patients with Hodgkin's disease treated with methyl-hydrazine as compared to 39 of 47 given nitrogen mustard and 29 of 45 with vinblastine.[13] There was no cross-resistance between these agents.[18] The median duration of remission with methyl-hydrazine is reported as 3.3 months, again briefer than with the use of the alkylating agents chlorambucil and cytoxan.[7,13] The toxic effects of methyl-hydrazine include severe nausea and vomiting, often necessitating alterations in dosage and cessation of therapy, hematopoietic depression, and evidence of central nervous system depression.

The tumor-inhibitory antibiotics that have received the widest clinical trial are the actinomycins and streptonigrins. Their anti-tumor effects in Hodgkin's disease and lymphoma are described by several investigators, although the duration of their effects and frequency have not been extensively reported.[28-30] There are, however, occasional instances of remission extending over six months. The disadvantage of these agents is the broad spectrum of toxic effect; that is, hematopoietic, gastrointestinal, mucous membrane, occasional pigmentary change and alopecia. Their role in the terminal management of lymphoma is certainly a restricted one, probably confined to patients who are refractory to the above mentioned agents.

When cortisone and ACTH first became available for clinical trial, the lympho-proliferative diseases were an area of therapeutic interest.[31] Most authors have concluded that benefit is impressive but transient, and the complications are frequent.[32-34] The use of corticosteroids is confined to instances in which there is no further response to x-ray or chemotherapy, and in patients in whom the course is complicated by bone marrow complications leading to anemia and/or thrombocytopenia. In Hodgkin's disease and reticulum cell sarcoma, tumor regression occurs in 10-20% of cases; in lymphosarcoma regression occurs in the majority of patients.[32,35]

Massive doses of prednisone (500 mgm—1 gm daily) are capable of eliciting clinical improvement in terminal lymphoma cases, but the period of improvement generally persists as long as the high dose is maintained. The toxic reactions have been so impressive (infections, diabetes, psychotic episodes, gastric or intestinal ulceration) that this form of therapy is a heroic measure useful only to meet a desperate situation.[35]

The objectives of the treatment of advanced lymphoma are to suppress the manifestations of the disease, to control its complications, and to provide the support necessary for the patient with a debilitating, fatal disease. When specific therapy is not practicable, the fever of lymphoma may be controlled with salicylates, steroids or with aminopyrine. Although aminopyrine may induce agranulocytosis, it is a worthwhile risk in a terminal patient with fever unresponsive to other measures. Intractable pruritis can also be treated with supportive measures when specific chemotherapy is ineffective. Prednisone may be helpful, or a combination of benadryl with salicylates given at regular intervals. Small intravenous doses of morphine (10 mg) also give rapid relief of pruritis, and merit consideration in terminal cases. Hypnosis has also been of benefit.

In the management of pain in terminal cases, anxiety often contributes to the patient's discomfort. Sedatives or tranquilizers may decrease the requirement for narcotic analgesia. If the patient's condition suggests a life expectancy of 6 months or longer, neurosurgical procedures, such as cordotomy, are worthwhile considerations. Otherwise, adequate use of potent narcotics, alone or with potentiating agents such as phenothiazine or pyribenzamine is essential. Other supportive measures, such as prompt investigation and treatment of infections, correction of anemia, and treatment of hyperuricemia and hypercalcemia when present, contribute substantially to the comfort of the patient. Supportive medical measures, such as treatment of infection, anemia, bleeding and effective analgesia may provide the most substantial clinical benefit to terminal lymphoma patients.

The compassion, understanding and moral support of the physician enable the patient to bear the consequence of debilitating neoplastic disease. It is a challenging and demanding responsibility.

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Use rauwolfias with caution in patients with history of peptic ulcer. Rauwolfias with anesthetics may produce hypotension and bradycardia. Discontinue Enduronyl two weeks before elective surgery. Consider vagal blocking agents during emergency surgery. In epilepsy, adjust anticonvulsant dosage. In electroshock, shorten stimulus strength and duration. In occasional patients with depressive tendencies, rauwolfias may precipitate severe mental depression that usually disappears when drug is stopped.

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Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804438R

ABBOTT

TM-TRADEMARK

THE PRESIDENT'S PAGE

I had been in office but a few hours when I received a long letter from a woman who expressed great concern about the lack of compassion of the present day doctors. I am sure she was not intending to indict the whole medical profession, but she certainly left no doubt that she felt that there has been a gradual weakening of the personal interest which was so much a part of the practice of medicine in the past. I rather wished this lady had been in the audience at the Annual Dinner of the Society when I made a plea for an increase in concern by doctors for their patients. Indeed, there were many things in her letter with which I agreed.

I happen to be one of those who believes that medicine is a profession and not a business. There are many aspects of the practice of medicine which set it apart from all other occupations. One of the most important of these is the close personal relationship which exists between the doctor and his patient. The success of the treatment does indeed often depend on this relationship, with the by-product of absolute trust in the physician. One may criticize the medical profession, but never his own doctor.

Doctors today are extremely busy people. Many days do not seem to have hours enough to do all that is asked of them. The tensions of being responsible, in many instances, for life itself do not make for a calm and unhurried inquiry into the complaints of some whom, one might well consider, are responsible for their own difficulties. It is all too easy in such cases to turn away from such patients since it is often not a medical problem at all. These are the times when the doctor must remember the obligations of his profession.

It can probably be safely said that the great majority of those men who decide to make medicine their life work do so because they want to treat the sick. I feel this very strongly. It is doubtful if there is a thrill which equals the one the young doctor feels when he successfully treats his first patient.

There are many today who insist that the practice of medicine is a business—not a profession. Medicine could be made a business if the personal touch were removed. We must all do our utmost to see that this does not happen. The compassion of the thoughtful and concerned physician for his patient denies this concept and effectively refutes it.

Keep medicine a profession. It is up to each one of us. The future is in our hands. We must not fail.

NORMAN H. GARDNER, M.D.

FROM THE GENERAL MANAGER'S OFFICE

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SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, May 15, 1968

I. Attendance

Members present were: Drs. Gardner, Martin, Grendon, Weber, Jr., Brandon, Abbot, Fabro, Bradley, Rogol, Cramer, Farrell, Egan, Petrie, Spitz, Purnell, Shepard, J. M. Grant, Nemoitin, Johnson, McDonald, R. F. Grant, Pelz, Granoff, Wilson and Palomba.

Also present were: Mrs. Lindquist, Mr. Villano and Dr. Richards. Members absent were: Drs. Caplan and Roch.

II. Organization

The President, Norman H. Gardner, called the organizational portion of the meeting to order, made introductions of the new and carry-over Council members, and asked for nominations for the office of Chairman of the Council for 1968-69. Since there was but a single nomination made, it was VOTED to close the nominations and direct the Secretary to cast one vote for Steven J. Martin, Hartford, as Chairman for the coming year. Following his election, Dr. Martin thanked the members for their confidence in him and assumed the chair.

III. Routine Business

Life Membership

It was VOTED to approve applications for Life Membership received from the following eligible Active Members of the Society:

Donald E. Tinkess, Greenwich (FMCA)—1968
Peter W. Fiskio, New Haven (NHCMA)—1968
Joseph A. Groark, New Haven (NHCMA)—1968

Committee Resignations and Appointments

It was VOTED to accept, with regret, and thanks for the past services, the resignation of Gordon C. G. Thomas, Stamford, as a member of the Committee on National Legislations and of the Committee on Public Relations. Dr. Thomas is leaving the State.

It was further VOTED to appoint replacements for Dr. Thomas on these Committees as follows:

(a) To the Committee on National Legislation: Edward A. Kamens, Bridgeport

(b) To the Committee on Public Relations: John L. Meyer, II, Thompson

Review and Appointment of Council Committees

(a) After making appropriate changes in the memberships of a number of standing and special committees of the Council, it was VOTED to appoint these committees for 1968-69.

(b) Since there has not been rotation of the Annual Meeting of the Society through the several county areas in recent years (1962-68), no county association Committee on Arrangements was appointed. Instead, it was VOTED to direct the President to appoint an Ad Hoc Committee on Annual Meeting Arrangements; to name the chairman thereof; and to include among its membership the following: The President, the Treasurer, the Speaker and Vice-Speaker of the House of Delegates and the Chairman of the Committee on Program of the Scientific Assembly, with the staff serving ex-officio. The task assigned to the Ad Hoc Committee will be to review our experience, including costs, with all component functions of the 1968 Annual Meeting and to make recommendations to the Council concerning arrangements for all component functions planned for the 1969 Annual Meeting.

(c) Since the Bylaws adopted by the House of Delegates on May 1, 1968 calls for the election of a Judicial Committee by the Council (replacing the previous Committee on Preliminary Study of Censorship Questions), it was VOTED to request the Committee on Preliminary Study of Nominations to make recommendations to the Council concerning qualified nominees for election to the Judicial Committee in accordance with the Bylaws. The CPSN is composed of the President, as non-voting chairman, and one Councilor or Associate Councilor from each of the component County Medical Associations.

(d) Since the Ad Hoc Committee on the Corporate Practice of Medicine has been inactive for several years, and contemplates no further studies at the present time, it was VOTED to discharge the Ad Hoc Committee with thanks.

(e) Concerning CSMS representatives on the State Planning Council for Hospital and Medical Facilities, it was VOTED to accept with regret, and thanks for past service, the resignation of Karl T. Phillips, Putnam, and to appoint David S. Hastings, Stafford Springs, as his replacement. The second CSMS representative on the Planning Council is William Mac Shepard, Putnam.

(f) It was VOTED to request the co-chairmen of the Ad Hoc Committee to Study Health Care Problems of the Poor to hold one or more meetings of the Committee in the near future and report to the Council its pertinent findings to date.

Date of Next Meeting

The next meeting of the Council will be held on Thursday, June 27, 1968, starting at 2:00 P.M.

IV. Old, New And Special Business

Report—Committee on Allied Medical Services

Hilliard Spitz, Chairman of the Committee, filed a report on several matters which have been discussed with representatives of nurses organizations. The report was acted on as follows:

(a) *Concerning a Request for CSMS to Recognize Licensed Practical Nursing as a Profession:* It was VOTED to receive this portion of the report as information, and to indicate to the source of the request that while the Society recognizes the contributions made to patient care by Licensed Practical Nurses, there is no precedent for the Society to pass judgment on the professional status of any calling except that of Doctor of Medicine nor any informed basis on which to attempt to set such a precedent to set such a percedent with reference to LPN's at this time.

(b) *Concerning the "Team Approach" to Medical Care:* It was VOTED to accept this portion of the report and to approve the Committee's recommendation that the component County Medical Associations be urged to establish liaison with representatives of nursing at local level for the purpose of exploring jointly the legal responsibility of both the physician and the nurse in "team" medical care in which the nurse carries out what are basically medical procedures at the direction of and/or under the supervision of the physician. The names of responsible representatives of nurses organizations in various parts of the State may be obtained from Miss Eleanor Lundblad, R. N., Executive Director, Connecticut Nurses' Association, 221 Sisson Avenue, Hartford, Connecticut 06105.

Connecticut Regional Medical Program

(a) It was VOTED to accept a report filed by E. Tremain Bradley, Norwalk, who, as an "Ad Hoc Committee of One", has had several meetings with the Program Coordinator of CRMP and his staff concerning possible ways in which the Society could play a fuller and more official role in the development of the Regional Medical Program. It was further VOTED to approve a recommendation offered by Dr. Bradley as follows: That the Deans of the two medical schools in Connecticut be invited, by letter, to participate promptly in discussions with representatives of the Society to: (1) review and evaluate the goals of CRMP; (2) review and evaluate the structure of CRMP; and (3) develop a mechanism for the inclusion of both parties (the medical schools and the Society) on an equivalent basis at the top level of CRMP.

(b) It was VOTED to receive as information a progress report of Frank K. Abbot, Waterbury, that his Ad Hoc Committee to Study the (recent) CRMP Grant Request is beginning the study assigned to it and expects to make a substantive report in the near future.

(c) As a means of implementing the directive of the House of Delegates (Mas 1, 1968) that the Council "seek from CRMP a review and evaluation of the latter's goals and structure", it was VOTED to direct the General Manager to send a letter to the Deans of the Yale and UConn Medical Schools which reports to them the action taken by the House and asks that they consider favorably developing a mechanism by which they and representatives of the Society may meet jointly to discuss the "goals and structure" of CRMP and to review and evaluate same. This liaison could be established directly with the Council, or, if preferred, be arranged with a smaller group of CSMS representatives on a preliminary exploratory basis. It will be noted that this action is in keeping with the recommendation offered by Dr. Bradley in (a) above.

Communication—NHCMA Member re Blue Plans

It was VOTED to refer to the Committee on Third Party Payments, for study and report, a lengthy communication from an NHCMA member concerning alleged shortcomings in the benefits coverage provided in Connecticut by both Blue Cross and Blue Shield. In essence, the member finds that in order to have the patient qualify for a number of benefits under both programs, unnecessary hospitalization and other unnecessary costly adjuncts are required.

Report—Representatives to Connecticut Health League

It was VOTED to receive as information a report filed by John J. Scanlon, Norwalk Chairman of the Society's three-man representation to the Connecticut Health League. In brief, the report covers the March, 1968 Annual Meeting of the Connecticut League at which the problems of "reaching the hard to reach" (in terms of transportation, home care, etc.) among disabled, feeble and underprivileged patients was the theme.

Requests for Expenditures

Actions were taken on requests for expenditures as follows:

(a) It was VOTED to authorize payment of 1968 membership dues to the Council of New England State Medical Societies in the amount of $150.

(b) It was VOTED to allocate an additional $200 to the 1968 budget of the Conference Committee with the Connecticut Bar Association, to cover anticipated costs of several meetings planned for the future.

(c) It was VOTED to authorize the Ad Hoc Committee to Study the Problems of Abortion, Voluntary Sterilization and Artificial Insemination to consult with the Society's legal counsel, Wiggin and Dana, New Haven, and to authorize the expenditure of up to $200 for such counselling. The Ad Hoc Committee wishes to obtain clarification of the provisions of existing Connecticut Statutes which have bearing on the matters under study. Anticipated legal costs in excess of this amount are to be submitted to the Council for prior approval. It was further VOTED to advise the Ad Hoc Committee of the availability of the Conference Committee with the Connecticut Bar Association, and to suggest that consultation with that Committee might prove to be of value.

(d) It was VOTED to reaffirm the Council's previous ruling concerning payment of usual expenses to members authorized to attend meetings of the AMA House of Delegates (the President, the President-Elect, 3 Delegates and 3 Alternate Delegates), and not to approve a request for such reimbursement submitted by a member not holding any of those offices at the present time.

(e) It was VOTED to authorize the Ad Hoc Committee to Study Hospital Costs and Related Matters to spend up to $600 for the purpose of engaging a part-time secretary-accountant to assist the Committee in its study of hospital cost accounting ledgers and in the preparation of its report.

Actions of the House of Delegates, May 1, 1968

(a) A resolution adopted by the House of Delegates (introduced by the Fairfield County Medical Association), urged that "the Governor's Advisory (Health Planning) Council to the P.L. 89-749 (Comprehensive Health Planning) program communicate with the Society with regard to assuring adequate and effective representation of practicing physicians in comprehensive health planning". As a start toward implementing the goal of the resolution, it was VOTED to request the President and the Present-Elect to confer informally with State Health Commissioner Foote and, if desirable, Governor Dempsey regarding the possibility of increasing the number of practicing physicians on the Planning Council. Presently, nine members of the Society have been appointed by the Governor to the Planning Council but, of these, only one is primarily a practicing physician. The P.L. 89-749 legislation provides that a majority of the Council must be public members (not connected with the provision of health services).

(b) There being apparent widespread confusion concerning the May 1, 1968 action of the House of Delegates with regard to the Council's attempts to implement the 4/27/65 resolution of the House on the admission of clean surgical (not just gynecological) cases to obstetrical floors, it was VOTED that it is the sense of the Council that implementation of the subject 1967 resolution *not* be pursued further at this time.

Report on RVS—Committee on Third Party Payments

Through administrative error, this report was not presented to the Council prior to the annual meeting of the House of Delegates—as expected by the Committee. The matters reported on were two in number: (1) Recommendations to make changes in the unit values assigned to certain types of office procedures (visits) under "Medicine" in the RV Schedule, and (2) recommendations to make changes in coding and unit values under "Surgery (Integumentary System)" in the RVS which have been proposed by the CSMS Section on Dermatol-

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ogy. Corollary to the report was a communication from the Connecticut Academy of General Practice protesting the changes in the unit values of office procedures recommended by the Committee. It was VOTED to approve the changes recommended under "Surgery (Integumentary System)", and to transmit these to the next meeting of the House of Delegates with the recommendations that they be approved by the House. It was further VOTED to refer the changes recommended under "Medicine" back to the Committee on Third Party Payments for reconsideration in the light of the questions and dissatisfactions raised by the CAGP.

Communication—Committee on Medicine and Religion

It was VOTED to receive as information, and with thanks, a letter from Francis W. Helfrick, Chairman of the M & R Committee, in which he expressed appreciation for the support given by the Council and the staff to the M & R panel program which had been held most successfully in conjunction with the Annual Meeting of the Society in Hartford, April 30, 1968. It was further VOTED to commend Dr. Helfrick for the high quality of his remarks on the occasion of opening the program, and to commend Dr. Paul B. McCleave, LL.D., AMA Department of Medicine and Religion, for the excellence of his service as the program's moderator.

Communications re Medicare B

Communications which have been received from several members of the Society were reviewed, the communications expressing varying degrees of dissatisfaction with Connecticut General's policies concerning the payment of "usual and customary charges". It was VOTED to instruct the CSMS component of the CSMS-CG Liaison Committee on Medicare B to meet separately, at suitable intervals, to consider these and similar complaints and to develop suggestions as to needed new policies or changes in existing policies to present to the CG representatives at subsequent joint meetings.

Hospital Planning vs. Planning Hospitals

Having received documented information from Sidney L. Cramer, HCMA Councilor, that there is a marked difference of opinion between administrators and trustees of hospitals and a number of public and voluntary agencies in the State having to do with hospital planning as to the direction hospital building and expansion should take to meet the needs of the future, it was VOTED to make this controversy the subject for the next Conference of County Medical Association Officers and to arrange for a panel of speakers qualified to speak on these opposing points of view. It is Dr. Cramer's feeling that physicians and their organizations at all levels should play an active role in resolving these differing concepts, in order that the proper interests of the profession and the public may be served best at a cost commensurate with what is actually needed to provide adequate hospital beds and services to all communities in the State, now and in the future. In brief, the hospital planners advocate that urban hospitals should expand their outpatient facilities and that increases in bed capacities should be authorized only for suburban institutions. Conversely, hospital administrations in Hartford and cities of comparable size advocate that facilities of all types be centralized in large urban areas.

COMPAC

It was VOTED to receive as information a communication from the Board of Directors of the Connecticut Medical Political Action Committee, which reported that the AMPAC-COMPAC booth at the recent Annual Meeting of the Society had been well patronized and that quite a large number of potential new COMPAC members were being contacted as a result of their having expressed an interest in joining to those manning the booth. On Tuesday evening, May 21, 1968, COMPAC's annual membership meeting will be held, at which meeting the COMPAC bylaws are planned to be amended so as to add five at-large members to the Board of Directors—including the President, President-Elect and Immediate Past President of CSMS.

Invitation to Medical School Deans and Others

On recommendation of E. Tremain Bradley, Councilor-at-Large, it was VOTED to extend an invitation to the Deans of the UConn and Yale Medical Schools to join the Council as guests at each of the next six meetings of the Council; to send them agendas for the meetings in advance; and to mark items on the agendas which are felt to be of special interest to the Deans and on which their comments are especially invited. Dr. Bradley has had continuing contacts with Drs. Patterson and Redlich and believes they would welcome this opportunity to establish and maintain continuing liaison with Society.

It was further VOTED to extend a standing invitation to Orvan W. Hess, New Haven, Medical Director of the State Welfare Department, to join the Council at any or all of its meetings. Dr. Hess has served the Society in many capacities, including Secretary, President and Councilor-at-Large.

Communication re Ear Piercing

In a communication addressed to the Council, an HCMA member states that he, his local Health

Director and the State Commissioner of Health all consider the procedure of ear piercing to be the practice of medicine and that its performance by those not licensed to practice medicine endangers the public health in several major ways (bleeding, local and systemic infection, etc.). The State's Attorney General, however, has ruled that ear piercing is *not* the practice of medicine according to the provisions of the Medical Practice Act. The Attorney General refers to the precedent established by tattooing, which required the enactment of a special statute to define it as the practice of medicine and to limit its performance to doctors of medicine or other trained persons working under their supervision and responsibility. It was VOTED to refer this matter to the Committee on Public Health for study and report as to whether the Society should introduce and/or seek the enactment of a similar special statute with regard to ear piercing at the 1969 General Assembly. For practical purposes, it is the Council's intention that such a statute would be limited to commercial and for-profit areas and not attempt to include occasional performance of the procedure by a relative or friend of the "patient".

Communication re Legislative Counsel

In a letter addressed to the General Manager, Attorney Joseph P. Cooney, Hartford, inquired whether the Society is planning to retain him as legislative counsel for the period January 1, 1968-December 31, 1969. Since all aspects of plans for the Society's legislative program for 1968 and beyond are still under study, and have not yet been finalized, it was VOTED to inform Mr. Cooney that it is not possible for the Council to give him a definitive answer to his inquiry at the present time—and perhaps not until the late summer or early fall; also, to thank Mr. Cooney for the excellent services he has rendered to the Society and its legislative committees in prior years.

Report—Ad Hoc Committee on Recognition for CSMS Service

It was VOTED to accept a report (given verbally) by E. Tremain Bradley, Norwalk, Chairman of this Ad Hoc Committee, which recommended a series of procedures by which recognition for service to the Society by CSMS officers, County Councilors and Associate Councilors, etc. will be made by presentation of appropriate certificates and/or gifts to such members upon completion of their prescribed terms of office, and recommending that a Committee consisting of the Immediate Past President, the Treasurer and the General Manager be established "to attend to these matters". Separate procedures are to be followed with respect to the President at the time of his inauguration, and to the Chairman of the Council at the termination (annual?) of his Chairmanship. A mimeographed copy of the Ad Hoc Committee's report will be sent out with the agenda for the next Council meeting as information, but, unless reconsidered and amended, will stand as accepted at this meeting.

Communication—Senator Abraham Ribicoff

Stevens J. Martin, Hartford, apprised the Council that he had received from Senator Ribicoff, accompanied by a personal letter, three copies of the verbatim proceedings of the first hearing on "Health Care in America" which had been held before his Subcommittee on Executive Reorganization of the Committee on Government Operations on April 22, 1968. It was VOTED to refer this document to the Committee on National Legislation for study and report to the Council. It was noted that, fortuitously, the Chairman of the Committee on National Legislation also chairs the Ad Hoc Committee on Hospital Costs and Related Matters.

Report—Committee on Investment of Funds

David A. Grendon, Sharon, Treasurer, reported for the Committee that no significant changes have been made in the investment program since the last report of six months ago.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on May 15, 1968. Detailed minutes of the meeting are on file at 160 Ronan Street, New Haven, for perusal by any interested member of the Society.*

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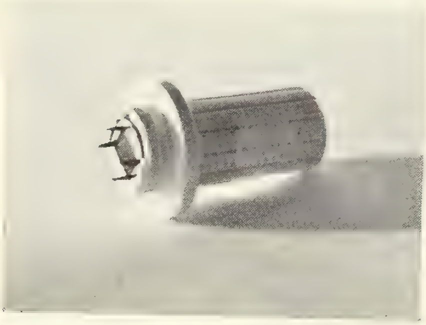

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Special Article:

ENDOCRINE AND METABOLIC EFFECTS OF PSYCHOTROPIC DRUGS: IV. HYPOTHALAMIC-PITUITARY-ADRENAL AXIS

Richard I. Shader, M.D., Donald R. Giller, A. B., and Alberto DiMascio, Ph.D.

The effects of emotional stress in man are of intimate concern to the physician. Although the administration of pharmacological agents to control extreme manifestations of emotional stress is common practice, little is known regarding the mode of action of such drugs in the human. In particular, their effects on the human hypothalamic-pituitary-adrenocortical axis, a most important pathway in stress states, remain poorly understood. Assessing these effects in man is not a straightforward task. Most of the literature, as expected, reports animal data, but to proceed from animal to man in this area of endocrine physiology is particularly difficult and deceiving, as we have suggested in earlier papers[1]. or example, one could incorrectly conclude from experimentation on the frog, that any effect a drug might have on ACTH release from the adenohypophysis would be reflected in the same direction in man in his aldosterone secretion. The error in this case arises from the fact that in the frog, aldosterone secretion is regulated primarily by ACTH, while in man ACTH at best serves in a permissive role—aldosterone being regulated primarily by potassium ion concentration and by the secretion of angiotensin II[2]. Even if one were cognizant of the differential physiology between animal and man, there would still be the difficulty of assessing some of the animal data, since older, more inexact, methods have often been used[3]. Lymphocytopenia, eosinopenia, and adrenal ascorbic acid depletion are now considered to be primarily of historical importance, since they are not sufficiently sensitive as indicators, lack adequate specificity, and have the disadvantage of evaluating pituitary activation but not inhibition. Adrenal weight is similarly confounded as a measure of ACTH secretion because of the imperfect association between adrenal size and functional capacity. Measurement of corticosteroid concentration in blood and urine is basically both sensitive and accurate, but does not adequately reflect short-lived or small changes in ACTH secretion.

We are unaware of any published reports which adequately document in human subjects the existence of clinically significant adverse effects upon the pituitary-adrenal axis from commonly prescribed psychotropic drugs. By contrast, rather drastic effects upon this axis have been noted in some animal studies in a variety of species. In studies of non-primates and primates, phenothiazine derivatives have been reported to increase, decrease or inhibit, or have no effect upon ACTH release from the pituitary[4-17]. Similarly, conflicting results exist with other classes of psychotropic drugs (e.g., benzodiazepines[18 19], thiaxanthenes[20], monoamine oxidase inhibitors[20-23], and tricyclic antidepressants[17 23]).

In view of some of the dramatic effects of psychotropic drugs on the pituitary-adrenal axis in animals, it is of interest that adrenal insufficiency or hyperactivity have not been attributed to the use of these drugs in man. A plausible explanation for this observation is the differential physiology between man and other species. For instance, following acute stress in the rat, there is a "stress nonresponsive period" or a period of relative nonresponsiveness[24-26]. However, there is no evidence that such a period exists in man[27].

There are, however, several reports that phenothiazines inhibit the normal adrenocortical response in man. Gold, *et al.*[28]. in a study on 20 psychiatric patients, reported that the normal two-fold rise in urinary 17-KGS levels following intravenous administration of mepyrapone was impaired by chlorpromazine (100 to 200 mg daily), perphena-

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MR. DONALD R. GILLER, *Research Assistant in the Psychopharmacology Research Laboratory; student at the Boston University School of Medicine.*

ALBERTO DIMASCIO, Ph.D., *Research Associate in Psychiatry, Harvard Medical School; and Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center.*

zine (24 mg daily), and fluphenazine (1.0 mg daily). Mepyrapone, a derivative of amphenone, selectively inhibits 11-β hydroxylation in the adrenal cortex, thus blocking the synthesis of biologically active cortisol—the normal feedback regulator of ACTH production by the adenohypophysis. The impairment of the 17-KGS rise was all the more striking, since this same dosage of chlorpromazine alone had produced a small rise in 17-KGS levels. In this same study, response to mepyrapone plus supramaximal doses of ACTH was reduced as much as the response to mepyrapone alone, indicating that the adrenals in these subjects were in some way rendered unresponsive to ACTH by these drugs. Similar results in psychiatric patients were obtained by Saarima, *et al.*[29], with daily doses of 300 mg of chlorpromazine for a period of up to 14 days. Also in psychiatric patients, CoTui, *et al.*[30], found that daily oral administrations of 300 to 450 mg of chlorpromazine to schizophrenic patients for varying periods was associated with a marked fall in blood hydrocortisone and urinary hydroxycorticoid values. Fotherby, *et al.* [31] reported an association between effect on adrenocortical function and dosage and mode of administration. Daily oral doses of 300 to 900 mg of chlorpromazine did not depress normal urinary 17-OHCS and 17-KGS levels in schizophrenic patients. However, 150 mg of chlorpromazine, given intravenously, was followed by a drop in these parameters. Christy, *et al.*[32], studying 8 schizophrenic patients, reported that pretreatment with 100 to 400 mg of chlorpromazine, given 0 to 12 hours earlier, blocked the normal plasma 17-OHCS rise in response to insulin-induced hypoglycemia. These authors suggest a block at the hypothalamic-pituitary level of the axis, since in their chlorpromazine-treated patients exogenous ACTH was able to effect adrenal response. Kothari, *et al.*[33], found that heat stress response was similarly blocked by chlorpromazine in schizophrenic patients. However, Sloane, *et al.*[34], found that chlorpromazine (25 mg intramuscularly) did not alter the urinary 17-OHCS increase usually seen with placebo injections in non-schizophrenic psychiatric patients, but that it did significantly reduce the increase from exogenous ACTH given intravenously.

In an excellent paper on the psychosomatic aspects of hyperadrenocorticism, Endicott and Gralnick[35], report the case of a 42-year old female with hyperadrenocorticism and marked anxiety, treated with chlorpromazine (50-150 mg q.i.d.). They report significant reduction in 17-KS, 17-OHCS, and urinary volume levels after chlorpromazine administration. However, they also caution that a reduction in anxiety and of other psychiatric symptoms is commonly observed following hospitalization, even if no special treatment is given. Nevertheless, these authors show convincingly that the failure of the patient's later increased depression and anxiety to produce a concommitant increase in these indices may be due to the hypothalamic blocking action of chlorpromazine, the drug thus reducing the cerebral cortex's influence on the hypothalamic-pituitary-adrenal system. The many possible relationships between adrenocortical functioning, mental processes, and mental illness are explored in depth by these authors. Rashkis and Harris[36], report the case of a schizophrenic male with a hyperadrenocortical diathesis. They noted a reduction in 17-KS and free corticoid levels following chlorpromazine administration, the dosage of which was titrated to the patient's "psychi comfort." However, the same patient was later shown to have a similar decrease in these indices during a psychiatric hospitalization in which medication was not used.

Two groups of investigators have noted that phenothiazines do not seem to affect adrenocortical response. Kallio, *et al.*[37], studying 67 psychiatric patients, found that chlorpromazine at usual therapeutic dose had little effect on plasma free 17-OHCS levels. Clear decreases were seen only after large doses continued over long periods of time. Sachar and Shader[38], after eluting thioridazine metabolites from the urine of chronic schizophrenics, found that thioridazine had no effect on urinary and plasma levels of 17-OHCS in the absence of patient anxiety. One methodological point deserves comment. The most commonly used method for determination of 17-OHCS is the Porter-Silber phenylhydrazine-sulfuric acid reaction. Betz and Ganong[9], state that chlorpromazine does not interfere with that method. However, Henneman and Pecket[39], contend that chlorpromazine does interfere with the specificity of this reaction. Only the Sachar and Shader study[38] eluted phenothiazine metabolites from the urine prior to making determinations of 17-OHCS, and no effect of thioridazine on hydroxysteroid excretion was found.

It is significant that there have been no reports in humans of any phenothiazine causing increases in any of the adrenocortical indices. The only report of any psychoactive drug causing such an increase was one by Simpson, *et al.*[40]. They found that WY-3457, a butyrophenone, increased total urinary 17-KGS excretion in 4 of 6 patients studied; in only one, however, did the increase reach statistical significance.

In work with monamine oxidase inhibitors on humans, saunders and coworkers[41], noted a decrease or inhibition of ACTH release. They reported that 50 mg of nialamide prevented the circulatory eosinopenia normally observed three hours after heat stress in male chronic schizophrenics. Significantly, exogenous ACTH and hydrocortisone effects on ACTH excretion were not suppressed; response to mepyrapone was, however, suppressed. The value of the eosinopenic index should be viewed with caution as suggested earlier. Non MAO-inhibiting antidepressants have also been said to decrease adrenocortical function. McClure[42], reported showing that imipramine and amitriptyline, both in doses of 150 mg daily, significantly lowered plasma cortisol levels in 5 depressed patients. McClure also stated that exacerbations of depressive moods, as noted by observers using a 5-point scale, directly corresponded to peak plasma cortisol levels, and suggested that the failure of plasma cortisol levels to fall within two weeks after initiation of such medication implies the need for a drug change. This report is difficult to evaluate, since heightened activity of the adrenal cortex has been observed in depressive reactions of various types[43]. Significant increases in urinary 17-OHCS excretion and elevations of plasma 17-OHCS have repeatedly been observed in studies of severe depressive states[44]. In light of this relationship between adrenocortical function and repression, the changes reported by McClure[42], may merely represent the decreases in adrenal activity which would be expected to follow clinical improvement. Gold, *et al.*[28], also reported that nialamide (100 to 150 mg daily), as well as meprobamate (1600 to 2400 mg daily) inhibited the rise in 17-KGS normally seen after mepyrapone administration in psychiatric patients.

Several investigators have proposed interesting mechanisms to explain some of the contradictions contained in the studies, especially the animal studies, cited above[45-48]. DeWied[49], suggests that chlorpromazine may at the same time activate and inhibit release of ACTH, and that these two phenomena can be separated by a lesion in the anterior median eminence of the hypothalamus. Interestingly, Ganong and Forsham[50], report that there is general agreement today that destruction of the anterior median eminence disrupts the function of the axis, and that corticotropin releasing factors apparently occur to a certain extent in the hypothalamus. In a previous paper[51], we concluded that chlorpromazine, the drug whose effects on the axis have been most studied to date, may depress ACTH secretion at two distinct levels: by acting on the median eminence of the hypothalamus to inhibit corticotropin releasing factors (CRF), and by acting on the pituitary to inhibit the release of ACTH directly or by blocking the susceptibility of the pituitary to CRF. Evidence suggests that chlorpromazine probably does not act directly on the cortex of the adrenal. ACTH depression might soon be overcome by the resulting reduction in peripheral adrenal hormones which would, in turn, stimulate a temporary increase in ACTH production. Continued high dose levels of phenothiazines might return the ACTH production to below normal levels.

It seems probable, however, that these mechanisms operate directly only in high-dose laboratory animal research. In the human, it is more likely that psychotropic agents alter adrenocortical function primarily by their effects on emotion and behavior, rather than through any direct action on the pituitary-adrenocortical axis.

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NINETEENTH CENTURY VIEWS ON THERAPEUTICS

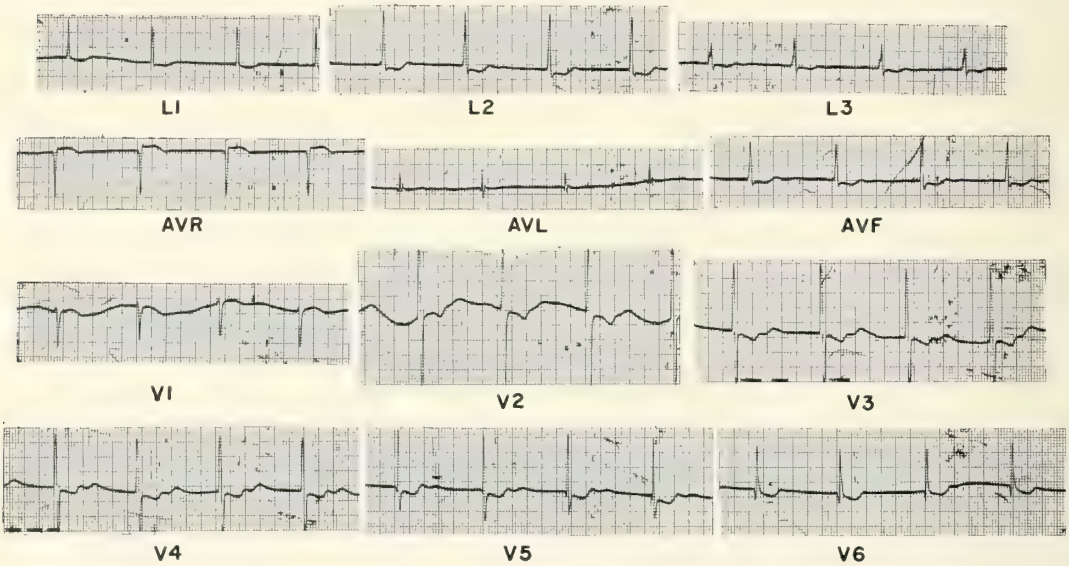
The intrinsic tendency of a disease to recovery, or otherwise, is to be considered with reference to the value of therapeutical measures. Knowledge of the natural history of diseases is important as the true point of departure for therapeutics. Much has been acquired, within late years, in this branch of knowledge, but much yet remains to be acquired. Diseases which were formerly supposed to tend to a fatal result, if not treated by means of active remedies, are now known to end generally in recovery, if let alone. Examples are acute pleuritis and simple pneumonitis. The importance of increasing our knowledge of the natural history of diseases, by collecting cases which have pursued their course without active treatment, is to be kept in mind by those desirous of contributing to the advancement of therapeutics, and opportunities of accumulating such cases should not be neglected, always provided that the welfare of the patient be not compromised by withholding measures which we have good grounds for believing will be useful.

It may be laid down as a golden rule in therapeutics that active measures of treatment are only to be employed in cases in which they seem to the physician to be clearly indicated. The severity of disease, and the danger of the patient, be they ever so great, do not alone constitute grounds for the employment of active measures. If they are not useful, they will be likely to do harm. —Flint, quoted by Mettler, C.C.: *History of Medicine*, F. A. Mettler (ed), Philadelphia: Blakiston Co., 1947, p. 464.

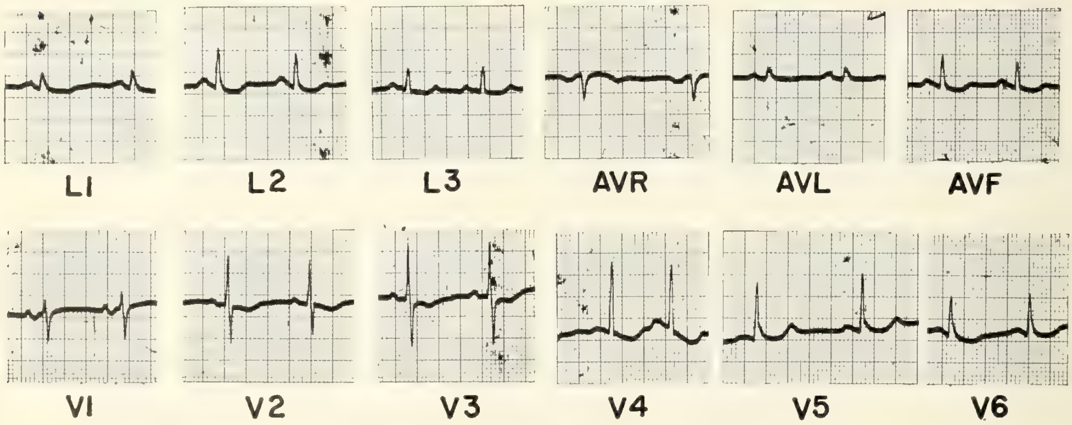
Electrocardiograms of the Month

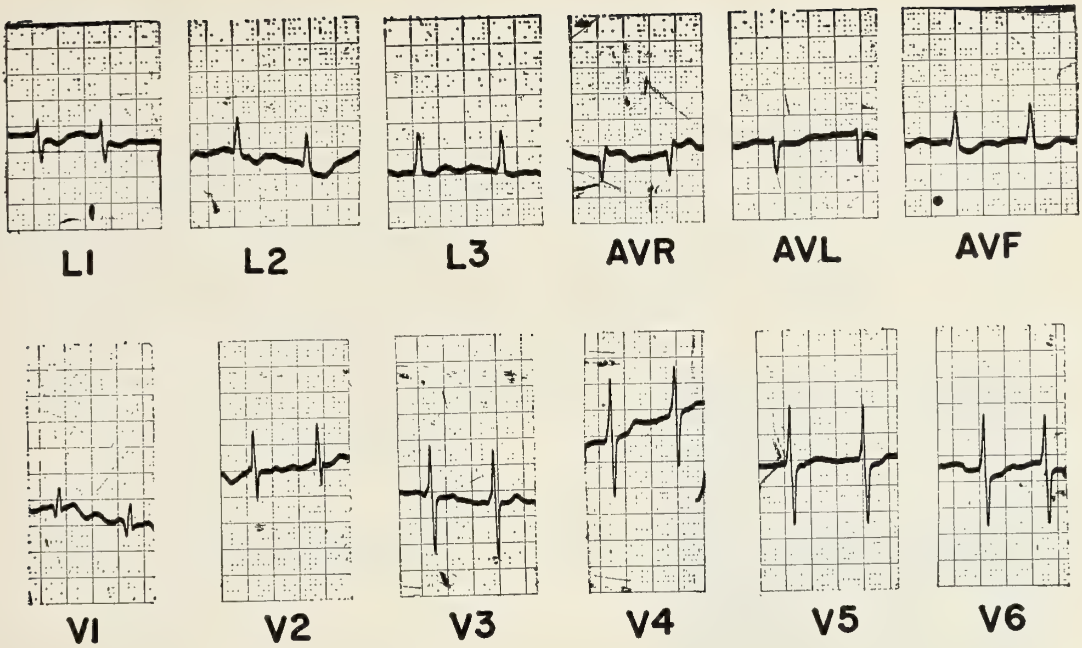
Montefiore Hospital and Medical Center
The Bronx, New York

Editors
IRA L. RUBIN, M.D.
Head, Department of Electrocardiography
JULIAN FRIEDEN, M.D.
Associate Head, Department of Electrocardiography



QUESTION 7. This is a routine tracing obtained on a seventy-five-year-old woman with a long history of arteriosclerotic cardiovascular disease. She had received 0.25 mg. of digoxin daily as well as intermittent diuretics. What is the interpretation?





QUESTION 8. The patient is a forty-year-old woman whose routine electrocardiogram is shown in tracing 3/30/66. The follow-up tracing, 12/23/66, was obtained on readmission to the hospital some nine months later. What is the interpretation?

Electrocardiograms of Month

ELUCIDATION

Question 7. The rhythm is perfectly regular. There are no P waves until one looks carefully in lead V_2. This lead shows small but definite P waves preceding each QRS by 0.24 second. The rhythm is therefore sinus with first degree atrioventricular block. The contour shows nonspecific S-T depressions in leads I, II, III, aVf, and V_2 to V_6. There are very prominent U waves in V_3 to V_5 which are consistent with a diagnosis of hypokalemia. These U waves may also be seen in patients with a slow cardiac rate who are receiving digitalis.

Question 8. The tracing dated 3/30/66 shows regular sinus rhythm with nonspecific S-T depressions in leads I, II, III, aVf and V_2 to V_6. There is a premature atrial beat in V_4. The P waves are notched suggesting possible atrial disease. In the tracing dated 12/23/66 the axis has shifted to a marked right axis deviation with a qR pattern in V_1. There is marked clockwise rotation in the precordial leads. The rhythm is now atrial fibrillation. These changes are characteristic of acute cor pulmonale. The patient was found at autopsy to have had multiple pulmonary emboli with mitral stenosis and insufficiency. There was a large left atrium.

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OBITUARIES

MORTIMER E. MORIARTY, M.D.
1898-1968

Mortimer E. Moriarty, M.D., 70, of 145 Park Street, Manchester, Connecticut, died May 2, at, the Manchester Memorial Hospital of a coronary thrombosis.

A native of Manchester, Dr. Moriarty attended Manchester schools, and graduated from Cornell University in 1922. He received his degree in medicine from Yale University School of Medicine in 1926.

After serving a two year internship at St. Francis Hospital, in Hartford, he began practicing in Manchester in 1928. Dr. Moriarty was Associate Physician at the Manchester Memorial Hospital from 1930-1956, and Chief of Medical Service from 1956-1963 at which time he was named Senior Physician of the Medical Staff.

Dr. Moriarty was one of the few local physicians who saw the Hospital grow from its infancy to its present status as one of the finest suburban hospitals in the country.

A strict disciplinarian and fine teacher, he insisted, above all, that the patient receive the best medical care possible. He was a U.S. Army Veteran of World War I, and a member of the Connecticut State Medical Society, the AMA, Manchester Medical Association, and the Yale Medical Alumni Association.

Dr. Moriarty was affectionately called "Mert" by his many friends. His silver white hair, his snappy blue eyes, and his quick Irish wit will be missed around the hospital and town of Manchester; adored by his patients, he will be missed as a friend, confessor, and as a true gentleman.

Survivors include his wife, Mrs. Mabel Johnston Moriarty, a son, Mortimer E. Moriarty Jr., a daughter, Mrs. John Ruddy, a sister, Miss Hannah Moriarty, and two grandchildren, all of Manchester.

I shall miss Mert as a loyal friend, a good teacher, and a student of good humor.

Let me close now with the "Old Gaelic Blessing":

May the roads rise with you.
And the wind be always at your back;
And the Lord hold you
In the Hollow of His Hand.

Joseph C. Barry, M.D.

CHARLES JOHN SATTI, M.D.
1895-1968

Dr. Charles John Satti, physician, surgeon, humanitarian, statesman and politician, died May 7, 1968, of cerebral thrombosis, at the Lawrence and Memorial Hospital in New London.

He was born December 4, 1895, in New London, educated in the city schools, and obtained his higher education at Rhode Island University and Yale Medical School.

He interned at King's County Hospital in Brooklyn, New York.

Upon entering practice in New London, he became an immediate success in surgery, medicine and obstetrics, often working until midnight, and after a few hours of rest up again for a delivery. For many years he was an active staff member of the Home Memorial Hospital. He was a Director of COMPAC since its inception.

C. John, as I liked to call him, loved his fellow man, and went out of his way to help those in need, whether medically so or in need of advice or employment.

He assisted several physicians in the New London area to get started in their practice, sending them patients and giving them practical advice, often seeing the patient as a consultant without fee.

Many persons now holding responsible positions, national, state, and civic were guided here by C. John.

His political career started with the New London Board of Education. He was a member of the

Ocean Beach Park Board, Secretary of State of Connecticut, Compensation Commissioner, Democratic State Central Committeeman, a member of the State Constitutional Convention, and was Democratic Town Chairman at the time of his death.

Fraternally he was a past exalted ruler of the Elks and very much interested in Elkdom.

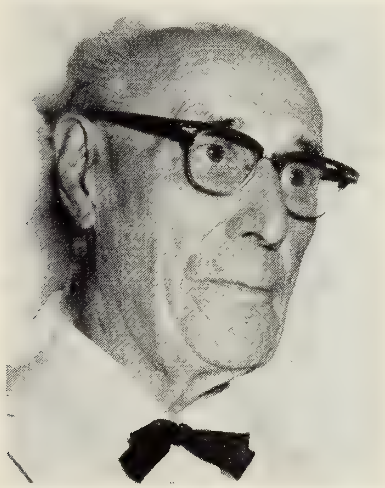
His wife Dorothy died in 1960. Living are two sons, Attorney C. Robert Satti and Dr. C. John Satti, Jr., of New London, and two daughters Mrs. Harry Butler of New London, and Mrs. Donna Nielsen of South Bend, Indiana.

Charles E. Dyer, M.D.

HOWARD GRANSON STEVENS, M.D.

1882-1968

Dr. Howard G. Stevens died at his home at 50 Bridge Street, New Milford, Connecticut on May 22, 1968, after a series of strokes beginning last Thanksgiving morning. He was 85.



Dr. Stevens was born in Norwalk, on August 24, 1882, the son of a lobster fisherman. He graduated from Baltimore Medical College (now the University of Maryland School of Medicine) in 1904. During his medical school years, Dr. Stevens spent vacations working and making rounds with Dr. Francis I. Burnell of South Norwalk, and soon after graduation he started his many years of general practice in Litchfield County, settling first in Cornwall Bridge. Shortly after he moved to West Cornwall. In 1907, he married Caroline Swift Hallett, and they moved to New Preston.

While in New Preston, Dr. Stevens served as health officer for the town of Washington and was medical examiner for the towns of Warren and Washington. He was also a member of the Washington School Board.

In 1921, Dr. Stevens moved again, this time to the big square Victorian house at the south end of the New Milford Green, where he lived and had his office for the rest of his life. While in New Milford, he served as health officer and school physician for the towns of New Milford, Sherman, Bridgewater and Roxbury. He was medical examiner for New Milford, Bridgewater, Roxbury and Warren. He served as medical advisor to the New Milford Visiting Nurse Association. He was a past president and honorary member of the staff of the New Milford Hospital. He was President of the Waramaug Medical Society at the time of his final illness. He was a member of the Litchfield County Medical Association, Conecticut State Medical Society, the American Medical Association, and the Connecticut Association of Medical Examiners.

Dr. Stevens was a charter member and past president of New Milford Lions Club, and a long-time member of the Litchfield County University Club. He was a devotee of ice-boating and a charter member of the Connecticut Ice Boat Association. He continued to enjoy this sport into his eighties. He also retained a love of boats from his boyhood days, and for many years kept a 31 foot fishing schooner at Norwalk.

Dr. Stevens' professional life was one of happy service to his patients and community, from the days when he traveled by horse and buggy or sleigh to isolated farms to deliver babies or treat pneumonia victims, up to last November. Warm, gentle, kind, understanding, and very wise, he was loved by his patients and honored by his colleagues.

He is survived by his wife, Caroline Hallett Stevens, of New Milford; a son, Francis H. Stevens of Ridgewood, New Jersey; two daughters, Mrs. Loring Miller and Mrs. Eliot Miller, both of Milford; two grandsons, four granddaughters, and two great-granddaughters and one great-grandson.

Jeffrey Ferris, M.D.

In Memoriam

Jarvis H. Gildersleeve, West Hartford; Johns Hopkins Medical School, 1919. Dr. Jarvis was a noted surgeon in the Hartford area for some 40 years. He was a former head of Hartford Hospital's medical and surgical staff. He was a member and past president of the Connecticut State Medical Society. He was also a member of the Hartford County Medical Association and the American Medical Association. Dr. Jarvis died May 30, at the age of 83.

Sweitzer, Donald S., Deep River, University and Bellevue Medical School, 1909. Dr. Sweitzer was a general practitioner in the Deep River area for 12 years. He was on the courtesy staff at Middlesex Memorial Hospital and had served as assistant health officer of Deep River. He was a member of the Middlesex County Medical Association and the Connecticut State Medical Society. Dr. Sweitzer died May 18, at the age of 77.

Placement Opportunities

INTERNIST urgently needed for community near Hartford, Connecticut. Rapidly expanding General Hospital serving a population of 30,000 needs internist to head the Department of Medicine and establish a private practice. Outstanding opportunity will be partially subsidized by the hospital and will be welcomed by friendly medical staff.

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ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Doctor's Office

Neil Auerbach, M.D., announces the opening of an office for the practice of internal medicine at 166 East Avenue, Norwalk.

Bernard S. Brody, M.D. and Eugene Rightmyer, M.D., announce their association in the practice of neurosurgery and neurology at 589 Boston Post Road, Madison.

Hubert S. Bush, Jr., M.D., announces the opening of a part time practice in general surgery at 66 Maple Avenue, Collinsville.

Bradford S. Colwell, M.D., announces the removal of his office for the practice of internal medicine to the Hamden Medical Center, 299 Washington Avenue, Hamden.

Charles C. Corradino, M.D., announces the removal of his office to 2 Church Street South, New Haven.

Edward Gerber, Jr., M.D., announces the removal of his office to 305 Church Street, Naugatuck.

Hans O. Gerz, M.D., announces the opening of an office for the practice of psychiatry at 75 Acer Drive, Middletown.

Morris E. Katz, M.D., announces the removal of his office to 108 New London Turnpike, Norwich.

Thomas P. Millar, M.D., announces the opening of an office for the practice of child psychiatry at 21 Broad Street, Stamford.

Samuel A. Robb, M.D. and Ely C. Wagshul, M.D., announce the removal of their offices from 69 E. Main Street and 95 E. Main Street to 285 Broad Street, Meriden.

Anthony D. Tramontozzi, M.D. and Larry Coletti, M.D., announce their association in the practice of general surgery and the removal of their offices to 108 New London Turnpike, Norwich.

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The auxiliary, in addition to its own programs outlined by the national organization and the assisting of the medical society during the year, is represented at several organizations involved in various health activities. We have delegates to COMPAC, the Conn. Health League, the Conn. Nutrition Council, and the Conn. Advisory School Health Council.

Mrs. Dewey Katz of Hartford, our representative for some years to the Conn. Advisory School Health Council and its present chairman, has prepared the following report of the council, including its formation, growing pains, and accomplishments since its inception.

The Connecticut Advisory School Health Council
A Resume

At the October 24th 1945 meeting of The Hezekiah Beardsley Club (The Pediatric Section of the Connecticut State Medical Society) a resolution was drawn up and voted, requesting "the Public Health Committee of the State Medical Society to form, in cooperation with the State Departments of Health and Education, a cooperative joint committee, including representatives of other interested agencies to interest public opinion in a school health education program; to formulate classroom programs, activities, standards, plans for establishing and carrying on such a program in all public schools; and to obtain, when it becomes desirable, such legislation and appropriation as may be required to put the program into effect".

This resolution was considered by the Connecticut State Medical Society's Council in November and referred to the Public Health Committee with a request to report on the matter at the semi-annual meeting of the House of Delegates. The favorable report of the Public Health Committee was accepted by the House which recommended that the State Medical Society Council appoint a committee to explore the possibilities for cooperative action as noted.

Doctor Joseph A. Hetzel was made chairman of this committee. A preliminary strategy meeting was called in January 1946 at which it was decided to ask the Commissioners of Health and Education to meet with the committee in March, and to augment the membership with several important people. At this meeting little was accomplished except an exchange of ideas. Both departmental representatives pointed to difficulties in the way of establishing a major health education program for the schools. These included the independent nature of the 169 local school boards, the lack of teachers to teach teachers to teach health. However, the presence of these and other obstacles did not diminish the conviction expressed by all present, that the need for health education was great and that returns from such instruction over a period of years would be of great value to the individual and to the state.

There followed a period of six years during which the Medical Society School Health Committee members gave a few talks before P.T.A., Medical Auxiliary and teacher groups. Interest in the education for health was increasing.

The Medical Society, ponderous though may be its ways, is a persistent body, and in 1952 its Committee on Public Health, spurred into renewed activity appointed an Advisory Committee on School Health. This body was charged with some 23 projects in the field, any one of which would require 5 to 10 years for solution. The committee was composed of representatives of the Society, the Departments of Health and Education, Yale School of Public Health, the State Dental Society, the Directors of Health, and school physicians. It first met in June 1952. At its February 10th 1953 meeting a plan for the formation of a State Advisory

School Health Council was produced and approved. The committee felt that the development of such a council would, in a large measure, solve many of the original problems with which the committee was charged. In September, 1953, the plan was reviewed in the School Health Committee of the State Medical Society. At this time, the suggestion for having co-executive secretaries from the State Dept. of Health and the State Department of Education for the State Advisory Council first appeared. This plan also enlarged the proposed membership to include, The State Department of Health, The State Department of Education, The State Medical Society, and its Woman's Auxiliary, The State Dental Association, The Association for Health, Physical Education and Recreation, The Boards of Education Association, The Chapter of the American Academy of Pediatrics, The Education Association: Classroom Teachers Section, The Connecticut Health League, The League for Nursing, The School Social Workers Association, The Elementary School Principals Association, The Local Directors of Public Health, The Parent Teachers Association of Connecticut Inc., The School Nurses Association of Conn., The School Superintendents Association, The Secondary School Principals Association, and The Yale University; School of Medicine: School of Public Health. This revised proposal was accepted by the two Departments and the Medical Society. Invitations were sent out by the Society for the first meeting of the Connecticut State Advisory Council on School Health to be held in February, 1954. The purpose of this Council was to be as follows: a. To bring together the representatives of official voluntary and professional organizations interested in school health, in order that they may share their accomplishments and programs and contribute to the development and improvement of school health programs in Connecticut, through cooperation and coordination. b. To determine problems and needs in the field of school health, make suggestions when indicated, identify problems and prepare recommendations for consideration by the commissioners of education and health.

Throughout this long eight year period certain people stand out for their leadership and ability. These include: Dr. Hetzel, Dr. Ira Hiscock, Dr. J. Harold Root, and Dr. Charles C. Wilson. Since 1953, the two co-executive secretaries, Dr. Ruth Byler and Dr. Martha Clifford, and her successors have been largely responsible for the direction and momentum of the State Advisory School Health Council.

At the first meeting of the Council held on February 26, 1954 Dr. Finis E. Engleman, Commissioner of Education, opened the meeting. He spoke on the legal role of the Department of Education, and concluded his remarks by stating that the Connecticut School Health Program showed little coordination and great unevenness. He welcomed an opportunity to work with the Department of Health and the Council. Dr. Osborn outlined the legal statutes and activities of the Department of Health noting the availability and willingness of his people to help in school health problems. He expressed pleasure at the formation of the Council and promised cooperation.

The second meeting of the Council was held in the Conference Room, State Dept. of Health on March 18, 1954. Dr. William J. Nolan, the delegate representing the Conn. State Superintendents Association, was elected the first chairman of the Council. A committee composed of Drs. Clifford, Byler, Schneider, and Mrs. Dewey Katz (chairman) was appointed to draw up an operating code. This was completed and adopted on September 16, 1954.

At the third meeting in October of 1965, the Council began its first project-the preparation of an Immunization Record. The Conn. State Medical Society Advisory Committee on School Health was asked to prepare the basic document which was then discussed and approved by the Council, and submitted to the Commissioners for final approval. On completion, this instrument was sent to all Directors of Health and School Superintendents with a covering letter signed by the two Commissioners. Thus was set a pattern which has been effectively employed many times since.

Other accomplishments of the Council include, besides many surveys and studies, the following published items: 1. A Suggested Self-Study Guide for Developing Local Health Policies, 2. Suggested Procedures for Protection and Release of Children While in School, 3. Recommendations Regarding Periodic Health Examinations for School Personnel, 4. Functions and Qualifications of A School Medical Advisor, 5. Basic Dental Health Recommendations, 6. A Statement to Schools Regarding Fluoridation, 6. Suggested Teacher Reference Guide on the Subject of Fluoridation of Public Water Supplies, 7. How Schools and Voluntary Agencies Can Work Together to Improve School Health Programs, 8. A Guide to Supplementary Health Education Materials of Voluntary Agencies-Working Together, Conn., Schools and State Level

Agencies, 9. Recommended Policies and Procedures for Tuberculosis Testing in Schools, 10. Report of the Committee on Family Life Education, and 11. A Teacher Reference on Smoking and Health.

These documents are being studied and used effectively throughout the State. Within the past year the Council has gone through the process of revising and updating most of the above publications, besides developing several new projects.

In November of 1955 the Council held its First Connecticut Conference on Physicians and Schools, it's Second Conference on November 14, 1957. Today, it is considering the need for its third Connecticut Conference on Physicians and Schools.

This is a record of accomplishment by the Council of which it may be proud. It represents a great expenditure of time and cooperative thinking. Yet, after 15 years, sound instruction in health is not yet a subject of prime importance in the curriculum of every school. As has been said before: "This is a problem of communication of ideas—a matter of education. We should use the full membership of all member organizations to do this—to influence local school and health boards.

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ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN CONNECTICUT 06511.

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Postgraduate Institute of The New York Eye and Ear Infirmary, 310 East 14th Street, New York, N.Y. 10003

Contact: Jane Stark, Registrar

October 5-6

Second National Congress on Medical Ethics

Drake Hotel, Chicago

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Speakers: F. J. L. Blasingame, M.D., Irving H. Page, M.D., J. Frank Walker, M.D., Chauncey B. Leake, Ph.D., Paul A. Freund, LL.B., Charles Forbes LL.B., and Milton D. Krueger

June 23-28

Educational Conference in Environmental Health

Sheraton-Park Hotel, Washington, D.C.

July 22-24

Air Pollution Medical Research Conference (AMA)

Denver-Hilton Hotel, Denver, Colo.

August 1-3

Conference in Dermatology

Aspen, Colo.

August 25-30

American Physiological Society (International Congress)

Washington, D.C.

August 26-29

Second Western Hemisphere Nutrition Congress (AMA)

Americana Hotel, San Juan, P.R.

BOOK REVIEW

HEREDITY, DISEASE AND MAN: Genetics in Medicine. Edited by Alan E. H. Emery, M.D. University of California Press, Berkeley and Los Angeles, 1968. 247 pp.

Reviewed by: LOUIS H. NAHUM

There has been tremendous advances in our knowledge of genetics mainly as a result of investigations in cytology and biochemistry. We can now understand much about the basic defects in many hereditary diseases. In consequence genetic units are springing up everywhere to advance our knowledge and sharpen our understanding of the causes of genetic disease. Mongolism, leukemia, cancer, mental retardation, abnormalities of sexual development are but some of the fruits of genetic research.

In this book the author, in clear and simple language, describes some of these advances and outlines some of the ways in which these problems have been investigated. The material is aimed for high school and college graduates so that they can form an idea about the applications and practical importance of genetics in clinical medicine. The practicing physician will find in it general information in the ten chapters on development of genetics, chemical basis of inheritance, chromosomal abnormalities, developmental genetics, inheritance of families, genetic factors in some diseases such as hypertension, diabetes, gout, hypercholesterolemia, pharmacogenetics, population genetics and natural selection, radiation and human heredity.

The last chapter on genetics and the physician is a must for every physician who deals with families, for in it are the simple facts that a physician should know about genetic counselling. What is most welcome is a list of references after each chapter and also a glossary of technical terms. One can read this book with his student son with much benefit to both.

ATLAS OF ROENTGENOGRAPHIC POSITIONS. by Vinita Merrill. The C. V. Mosby Company, St. Louis, 1967. 878 pp. $46.50 (Volumes 1, 2 and 3)

Reviewed by: RICHARD H. GREENSPAN, M.D.

This Atlas has been the standard reference book for radiographic technologists and schools of x-ray technology since its initial publication, almost 20 years ago. The appearance of the third edition is particularly welcome since, in a field such as diagnostic radiology, where changes in examinations and techniques are constantly occurring, "standard" textbooks rapidly tend to become obsolete.

This new edition has been significantly revised and brought up-to-date. Sections on protection against ionizing radiation, lymphangiography, and cardiac and peripheral angiography have been contributed by experts in the respective fields. New illustrations have been added and others have been rearranged for greater convenience of use. The labeling of various illustrative radiographs is particularly welcome. Many new x-ray positions have been added to the book and the section on the examination of the urogenital tract has been expanded greatly. Newer diagnostic procedures have been included, also.

A major revision of the section on skull radiography has been accomplished and a much more extensive description of pneumonencephalograms and cerebral angiograms is presented. The grouping of positions for skull roentgenography, along with the special procedures for examination of the intracranial contents in one unit, is a particularly welcome change. Appropriate bibliographic footnotes are included along with the text and, in addition, an up-to-date chronologic bibliography is given at the close of each volume.

The diagrams, photographs of patients in examination positions, and reproduction of x-ray are, in general, outstanding although the angiocardiograms chosen for illustrative purposes are not of the highest technical quality. The book is comprehensive in its coverage of routine radiographic procedures and reasonably complete in special x-ray examinations. Some of the highly specialized and newer procedures are not included, but the bibliography is sufficiently complete so that pertinent reference material to these procedures can be found. The author is to be congratulated on maintaining the balance between a description of practical x-ray technique and the science of x-ray technology, a blend that has characterized her Atlas from its inception. This new edition should have a place in all departments of Diagnostic Radiology and technologists' training schools.

OCULAR THERAPY, Complications and Management Volume II. Edited by Irving H. Leopold, M.D. The C. V. Mosby Company, Saint Louis, 1967. 139 pp. Illustrated. $11.00

Reviewed by: MARVIN L. SEARS, M.D.

This publication, the second of its kind, destills important pharmacologic information presented at national symposia held in 1964 and 1965, and delivers it in palatable fashion. The text is not exhaustive, but rather provides a good deal of current data on a variety of important therapeutic problems in ophthalmology. It is imperative reading for every practicing ophthalmologist.

The contents of the volume are divided into 13 short chapters, a number which portends evil for all therapists, as the reader soon learns. There is hardly a topical medication that does not have important toxic effects. Caution is properly emphasized throughout the text. One or two examples will suffice. Phospholine iodide, a highly effective anti-glaucomatous medication, is cataractogenic. Topical steroids in high doses may have the same potential, and, even in lower doses may increase the susceptibility of the cornea to fungus infections, elevate intraocular pressure in predisposed individuals, and give rise to a superficial keratitis with prolonged usage. One pharmacologic agent with high potential for ocular toxicity, not so frequently used by the ophthalmologist as by the pediatrician, is oxygen. The use of this drug in neonatal respiratory diseases must be monitored with indirect ophthalmoscopy of the young retinal vessels susceptible to the vasocontrictive effects of oxygen. Examination must be made frequently by the ophthalmologist to avert the disastrous effects of retrolental fibroplasia.

In addition to emphasizing the hazards of topically administered agents, expertly written chapters on the abuses of combined systemic and local therapy highlight the importance of eliciting a careful history of drug intake from a patient. Salt depletion is but one of the harmful consequences in store for the patient who receives anti-glaucomatous carbonic anhydrase inhibitors while he is medicated with other diuretics for other purposes, and so on. An excellent summary of the photosensitizing effects of phenothiazines upon the eye and skin is provided by Dr. Apt while new avenues for travel in the therapy of infectious diseases is ably discussed by Drs. Leopold and Kaufman, who indicate future possibilities for treatment of virus diseases and the devastating effects of pseudomonas and pyocyaneous endophthalmitis.

Any gaps in information organized within this book do not reflect upon the manuscript but rather upon our appalling lack of knowledge concerning the relationships between the effective therapeutic concentration of a topical agent and its penetration and metabolism within the eye. Continuous clinical research must be pursued to supply the practicing ophthalmologist with this requirement.

The Connecticut State Medical Society offers placement assistance through the Physician Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Cardiovascular physiology. Edited by Robert M. Berne, M.D. and Matthew N. Levy, M.D. The C. V. Mosby Company, Saint Louis, 1967. 254 pp. with 148 illustrations. $10.75

Cardiovascular Surgery 1967. American Heart Association Monograph Number 19. Edited by C. Frederick Kittle, M.D. American Heart Association, Inc., 44 East 23rd Street, New York, N.Y., 10010. 217 pp. $3.00.

The National Diet-Heart Study-Final Report. American Heart Association Monograph Number 18. Edited by the National Diet-Heart Study Research Group with the approval of the Executive Committee on Diet and Heart Disease. American Heart Association, Inc., 44 East 23rd Street, New York, N.Y., 10010. 428 pp. $3.50.

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Public Relations Notes

THE RECERTIFICATION OF PHYSICIANS (AND POLITICIANS, TOO)

by Lyon Steine, M.D.

For some time past I have been coming across references in various communications media to an interesting concept known as "Physician Recertification." This concept derives from the fact that so many derogatory articles have appeared in recent years in magazines and newspapers bearing such titles as "Why Some Doctors Should be in Jail," "Are Your Medical Bills Padded?" "Was Your Operation Necessary?" etc., etc. In all of these the doctor is described as a heartless, swindling, ignorant, conniving, crook, performing unnecessary operations and allowing his patients to die from a combination of ignorance and neglect; this has been repeated so often that the opinion-makers have now begun to believe their own propaganda. So we hear and read statements declaring in effect that doctors can be no longer trusted to keep up with the advances of "medical science" and that, to protect the health and lives of the public, all doctors should be reexamined and recertified as a precondition to the right to continue in practice. The implication here is that if some self-appointed group or panel of busybodies didn't keep after the doctors, they would all be treating sore throats with purges, emetics, blood letting, cupping and leeches.

The recommendation for recertification overlooks the fact that practically everyone with an illness of any severity is treated in a hospital. And the doctor in the hospital setting is closely watched by more kibitzers than a dog has fleas. He has a whole legion of other doctors looking over his shoulder and breathing down his neck. He has the Utilization Committee and the Record Committee and the Efficiency Committee and the Tissue Committee and half a dozen more watching him to make sure he pulls no boners.

Recertification would probably operate by means of some supervising board which would prepare an examination which every practicing doctor would have to pass in order to keep his license active and in force: such examinations to be given at fixed intervals of, say every five years. There is no denying the fact that an ill-trained doctor is a menace to public health and safety. Way back in the Middle Ages people recited a prayer—

A cibo biscoto	From food twice cooked
A medico indocto	*From an ignorant doctor*
Ab inimico reconciliato	From an enemy reconciled
A mala muliere	From an evil woman
Ab omni malo	From all evil
Libera nos, Domine.	Good Lord, deliver us!

My objection to recertification is not to the *idea* as such but to the fact that it doesn't go far enough. I should like to see it applied not only to physicians but also to lawyers, architects, engineers, teachers, in fact to all the professions. I would even like to see it applied to marriage. Think of the improvement in the relation between husband and wife that would ensue if every marriage were to be recertified every

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The author is a member of the Editorial Board of the Nassau Medical News. Reprint by permission of the author.

five years, such recertification to be granted only after re-examination of both parties by a designated Board. Just think of the hen-pecked husbands and of the neglected wives whose spouses would show a complete change of attitude if they knew that the marriage would "run out" at five year intervals subject to relicensure or annulment.

The greatest benefits to mankind however lie in the promising field of recertification of politicians. Most of us have a completely erroneous impression of politicians. We tend to consider them to be necessary nuisances at their best and necessary evils at their worst who clamor for our attention and our votes at election time and who ignore us during the intervals between. We tend to dismiss them with such comments during election campaigns as, "Thank Heaven all the candidates can't be elected," or "Praise the Lord we don't get *all* the government we are paying for," or "I can't possibly afford to pay for all the things the candidate wants to do for me"; we feel like the old lady in Vermont who, when asked whom she had voted for in the recent election replied, "I never vote. It just encourages *them*."

The fact is that politicians have much more power over our lives than we realize. I quote from a recent speech by Rep. Otto E. Passman—"Politicians have much to say about the kind of food you eat and the fabrics you wear. Politicians tell you when to fish and hunt and what you can catch and kill. Politicians control the medicine you prescribe for your patients. Politicians tell you whom to employ. They prescribe the rules, hours and pay of your employees. They are now telling you what color our employees shall be. Politicians tell you what part of your earnings you can keep and what part you must turn over to the government. On the average, the politicians are now taking 37 per cent of the people's earnings in surface and submerged taxes. The politicians follow you to the undertakers. And after the funeral he again takes over and claims a big part of your estate. So, in reality, the politician controls your life not only from the cradle to the grave, but also one step beyond the grave."

Such being the case I make the following suggestion: *all politicians shall be made responsible for their words and their deeds*. For example, a man running for public office declares in a public speech (as they always do) that if elected he will balance the budget without levying any additional taxes. He is elected and the budget (as is always the case) becomes more unbalanced than ever. He would be thereupon fined ten-thousand dollars, fired from his job and declared to be ineligible thereafter to hold public office by the appropriate Qualifying Board. This simple principle can be extended to apply to almost all political activity. For example, a legislator introduces a bill to achieve some laudable purpose, call it "A Bill to Reduce Crime in the Streets." His bill is passed and after a reasonable time has elapsed it is noted (as is usually the case) that there is more crime in the streets than ever. The legislator who sponsored the bill is then fined ten-thousand dollars, expelled from the legislature and declared ineligible to hold public office. Perhaps *all* those members of the legislature who voted *for* the bill could be automatically fined five-thousand dollars as accessories. . . .

The adoption of this simple plan for certification of politicians would accomplish, if nothing else, two highly desirable ends: it would make for much shorter and quieter political campaigns and would result in the enactment of far fewer laws.

NEW HAVEN COUNTY MEDICAL ASSOCIATION

The New Haven County Medical Association held an indoctrination meeting for fifteen provisory members at the Colonial House in Hamden, on Wednesday, June 5th. The candidates were addressed by Doctors Charles Verstandig, William R. Richards and Max Caplan representing New Haven County Medical Association, Connecticut State Medical Society and American Medical Association.

We were pleased to listen to the remarks of a very special guest, Dr. Frederick Redlich, Dean of the Yale Medical School. We hope his presence marks the start of long needed rapport between the medical school and the practicing medical profession. It was a good beginning.

Respectfully submitted,
H. A. LEVIN, M.D., Clerk

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Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

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NEWS

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ADVERTISING

All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by CONNECTICUT MEDICINE.

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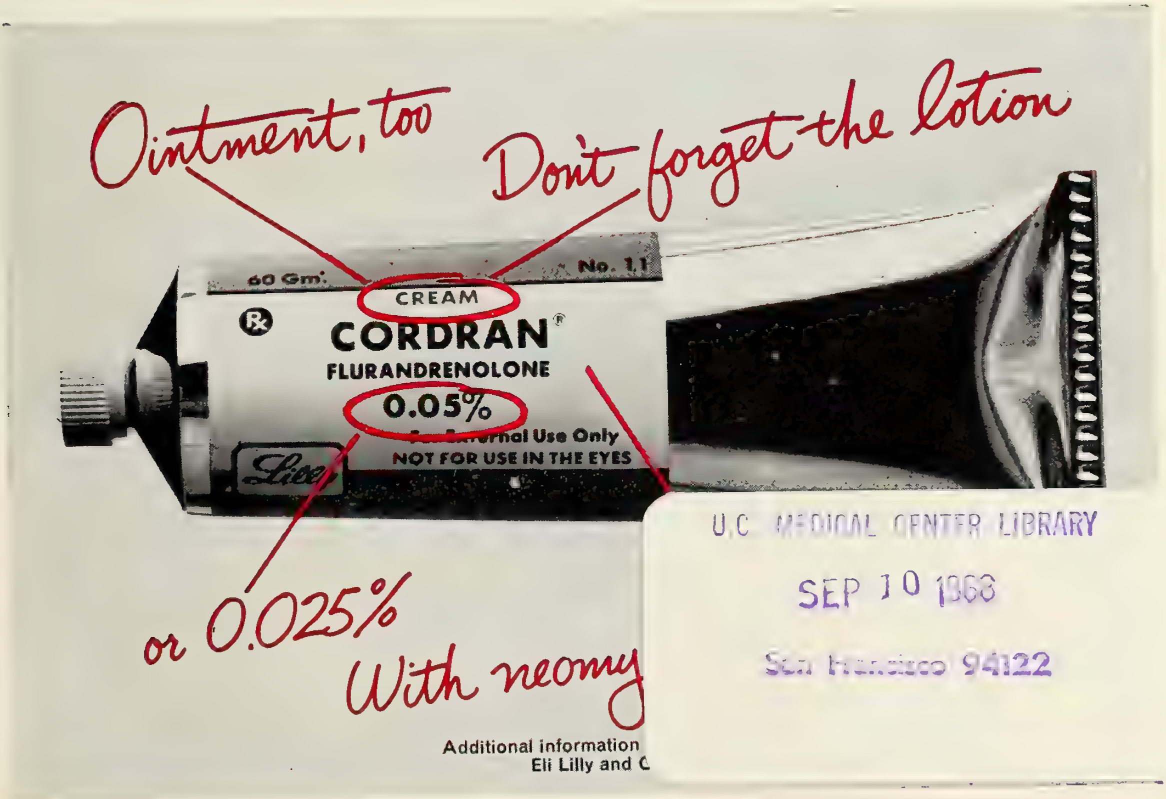
Connecticut Medicine

Connecticut State
Medical Journal

Volume 32/August 1968/Number 8

CHILD STUDY CENTER, YALE UNIVERSITY

Melvin Lewis, M.D. Guest Editor



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Literature on indications and dosage available on request.

References:

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Connecticut Medicine

AUGUST, 1968
Vol. 32/No. 8

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Connecticut Medicine

editorials

The National Institute Of Dental Research

Twenty years ago an act of Congress created the National Institute of Dental Research (NIDR) in recognition of the fact that dental disease is a threat to the nations health, well-being and productivity. In the intervening period there has evolved a generation of dental practitioners and researchers whose concepts of dental disease, dental practice and related research are so modified as to add an entirely new dimension to their functional role as health specialists.

In the earlier efforts of the profession to establish a separate identity in the field of health, the mouth was considered—mistakenly—a biologic entity. Largely through the influence of NIDR, dental science has moved from a mechanical to a biological orientation and the oral cavity is again looked upon as an integral component of the body. Dental science is now aligning itself with a broad front of basic sciences and as a result exciting progress is being made toward an understanding of oral disorders. At the same time dental science is increasingly providing information of fundamental importance to other fields of scientific endeavor.

Dental research has so extended the boundaries of oral biology that it is now totally inappropriate to restrict it to tooth and mouth. The biochemist is studying cross-linkages of collagen. The microbiologist is studying the polysaccharide coating of streptococci. The metallurgist is investigating the phenomenon of corrosion. The crystallographer is examining the structure of the apatite crystal. All are engaged in work of vital interest to dentistry. This statement can be expanded to include research of scientists from thirty discreet disciplines.[1]

That research involving the oral cavity must inevitably implicate a wide range of science disciplines becomes obvious when the total oral environment is considered. Anatomically the mouth includes all basic tissue elements. The penetration of the tooth through the oral mucosa is the only example of the loss of continuity of the protective layer of skin or mucosa which lines all body surfaces or cavities. The nature of the union between the soft tissue of the oral cavity and the tooth structure in an erupted tooth is anatomically unqiue as is the suspensory ligament by which the tooth is anchored in bone.

The salivary glands functioning under neural and endocrine control, excrete each day approximately 1500 ml. of fluid containing minerals, glycoproteins and enzymes. There is evidence in animals which also suggests an endocrine function of these glands. The oral cavity has a rich microflora which includes bacteria with a full range of oxygen dependency. Commonly present in the oral cavity are various dental restorative materials such as gold, silver amalgam and other alloys silicate cements and acrylic polymers. Often there is a measureable galvanic potential between dissimilar metals and the electrolyte containing saliva. Further complicating this environment are the drying and other effects of frequent exposure to outside air and the ingestion of foodstuffs and other materials representing a limitless range in terms of chemical structure and physical consistency. Temperature ranges from 0 to 60° C. occurring within seconds are commonly associated with the eating habits of Americans.

The first NIDR grants and training programs amounted to 1.78 million. Now in 1968 it has reached 30.3 million. It supports training grants to clinical investigators, so that more dentists are becoming trained in research techniques. It supports training of individuals who are not primarily identified with the dental profession especially in basic science disciplines. At present there are 100 professional investigators more than half of whom are trained at the doctoral level in fields other than or in addition to clinical dentistry. They carry out full time research leading to better control of oral disorders and to their prevention. Much of this research is clinically oriented but a substantial part seeks to provide a necessary underpinning of basic knowledge and takes off from the vantage points of pure biochemistry or microbiology or experimental morphology, genetics and other disciplines.

This multidisciplinary approach has resulted in an improved capacity to deal with dental ills giving rise in the process to a large body of information relevant to other health areas. Such "cross fertilization" is evident in the fact that of the ninety-three research projects currently being conducted by NIDR staff 78 per cent are being carried out in collaboration with researchers in other institutes. In a recent ten month period NIDR scientists contributed papers on original research to fifty scientific Journals. Both parallel and individual studies are being carried on in academic and non academic centers of research in many areas of this country.

With such important work going on in the field of health, Congress either has or is threatening to cut back appropriations for science research. We must all raise our voices against Congress's shortsighted policy in reducing financial support for research in medicine. If it does it will be turning its back on the future health and well-being of the people of this country.

L.H.N.

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Dietary Therapy And Cognitive Development In Phenylketonuria

Phenylketonuria (PKU) is a metabolic defect in which the infant is unable to use absorbed phenylalanine properly. He is unable to do this because he lacks a liver enzyme phenylalanine hydroxylase which converts phenylalanine to tyrosine. The resulting high concentration of phenylalanine in tissue fluids and especially the central nervous system leads to mental retardation in the untreated infant. Several workers discovered a diet low in phenylalanine that produced beneficial changes in PKU children and a modification of this diet is now widely used.

Initial clinical evidence suggested that mental retardation could be prevented if the diet were started in infancy. In response to the need for early diagnosis widespread screening programs were developed to allow identification and treatment during earliest infancy. Until recently then a simple syllogism has governed thinking and publicity about PKU and in fact a large number of other diseases of metabolism associated with mental retardation. The patient has too much or too little of some normal intermediate in his body fluids owing to an enzyme defect and this has led in some to mental retardation. The partial or complete removal of the offending material or restoration of an insufficient amount to normal will prevent this brain damage.

The efficiency of the diet low in phenylalanine has recently been challenged by Bessman[1] even though it has received broad clinical acceptance. Divergent points of view exist also regarding the optimal duration of treatment as well as the beneficial effects of the low phenylalanine diet in preventing mental retardation. The challenge to the accepted therapy originates in part from the occasional identification of untreated PKU children with normal intelligence. Then there are difficulties involved in conducting research on PKU because of the rarity of the disorder, its variability in clinical response and the complicating effects of sociologic factors.

Dobson's[2] study was designed to examine the intellectual abilities of patients as related to varying treatment conditions with an attempt to eliminate some of the biases that may have distorted previous research efforts. More specifically he wished to provide meaningful data concerning the following questions: what is the relation between the age at which a low phenylalanine diet was initiated and eventual intellectual abilities; what normative data can be accumulated concerning the intelligence and language of non-institutionalized children?

Apparently the low phenylalanine diet does not seem totally capable of preventing some brain damage even when instituted shortly after birth. Even when treatment was begun early and administered properly the patients mean I.Q. and Illinois Test of Psycholinguistic Abilities, scores were significantly lower than those earned by their parents and siblings without PKU. The children treated within one month after birth scored an average of 33 I.Q. points higher than those for whom treatment was initiated within their fourth and sixth years of life. Dobson concluded from his data that a consistent inverse relation exists between the present intellectual ability and age of dietary inception. However, even under ideal conditions some damage seems to occur and no guarantee of normal intellect can be offered.

The article by Dobson et al is one of the first clear signs that all is not well with the campaign of diagnosis and treatment carried on from 1963 when Massachusetts passed its compulsory screening law for PKU. Subsequently forty states have passed more or less stringent laws regulating medical activity in the diagnosis and in a number of states the treatment of PKU. At the International Symposium meeting in 1967[2] it was reported that PKU children treated with a diet deficient in phenylalanine before the third month of life achieved an I.Q. approximately 106-108. At this meeting treatment of children beginning at three months caused a twenty point higher level in I.Q.

whereas Dobson's group at the fourth month found it was eighty in twenty children.

As Bessman points out the testing was done four years ago at which time the diagnosis of PKU was much less rigid than at present and the syndrome of hyperphenylalanemia—a form of high blood phenylalanine without mental retardation was unknown. It is Bessman's view that environment alone has an influence on the PKU child to raise its I.Q. and that the reported claims of large improvement from the deprivation treatment alone can be fallacious.

Dobson's group, however, have performed a real service in revealing the sober view of the whole problem of the pitfalls in assessing the true value of deprivation treatment in PKU infants. There is room for more serious studies of this problem which has become a legal as well as a medical one. Perhaps the blood brain barrier varies in patients with respect to phenylalanine. This could account for normal brain function in some cases with hyperphenylalanemia in whom the blood brain barrier prevents excessive amounts of phenylalanine to enter the brain.

L.H.N.

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Ortho Molecular Psychiatry: II. The Concept Of Localized Cerebral Deficiency Diseases

Mental symptoms of avitaminosis sometimes are observed long before physical symptoms appear. The observation that the psychosis associated with pernicious anemia may manifest itself in a patient for several years before other manifestations of this disease became noticeable is given a reasonable explanation by Pauling.[1] If functioning of the brain and nervous tissue is sensitively dependent on molecular composition than is that of other organs and tissues, then the observed high incidence of B_{12} deficiency of patients admitted to a mental hospital suggests that mental disease may rather often be the result of this deficiency and suggests further that other deficiencies in vital substances may be wholly or partly responsible for many cases of mental illness.

The general principle follows that under certain circumstances a deficiency disease may be localized in the human body in such a way that only some of the manifestations usually associated with the disease are present. Suppose a person of unusual genotype has an especially great concentration of an enzyme in one body organ with essentially the normal amount in other organs. Through the action of such an enzyme the concentration of a vital substance of this organ might be decreased to a level much lower than that required for normal function. Under this circumstance there would be present a deficiency disease restricted to that organ as was already noted for ascorbic acid in schizophrenia.

The brain is an especially important case in point since here there are two compartments, blood and lymph on the one hand and cerebrospinal fluid and extracellular fluid of the brain and spinal column on the other. A vital substance could be destroyed in each of these reservoirs at a different characteristic rate. Even if the differences are small a decrease in permeability of the barrier or increase in metabolic rate of the substance, then the steady state concentration in the brain could become much less than that in the blood.[2] If this is so then the possibility exists of a localized cerebral avitaminosis or other localized cerebral deficiency disease.

Thus we envision the possibility that some human beings have a sort of cerebral pellagra or cerebral pernicious anemia. Pauling has long ago pointed out that every vitamin, every essential amino acid, every other nutrilite represents a molecular disease which our distant ancestors learned to control when it began to afflict them by selecting therapeutic diets and which has continued to be kept in control in this way.

The localized deficiency diseases described above are also molecular disease involving not only the original lesion, the loss of ability to synthesize the vital substance but also another lesion, one that causes a decreased rate of transfer across a membrane such as the blood brain barrier to the affected organ. There can also be an increased rate of destruction of the vital substance in the organ. And as in phenylketonuria an excessive accumulation of an essential amino acid phenylalanine due to absence of an oxidizing enzyme. There may also be some other perturbating reactions yet unknown.

Pauling thinks that the gene or genes involved in the schizophrenic regulate the metabolism of vital substances such as ascorbic acid, nicotinic acid,

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pyridoxin, B_{12} and other substances. The reported successes in treating schizophrenics and other mental illnesses by use of massive doses of some of these vitamins may actually be the result of successful treatment of a localized cerebral deficiency disease involving these vital substances, a sort of "multiple cerebral deficiency."

For the orthomolecular treatment of mental disease to be successful we need a thorough study of and attention to the individual such as is customary in psychotherapy but much less customary in conventional chemotherapy. In the course of time it should be possible to develop a method of diagnosis by measurements of concentration of vital substances that could be used as the basis for determining the optimum molecular concentration of vital substances for the individual patient. This should indicate the appropriate therapeutic measures to be taken. Since in some persons the possibility exists that the concentration of a vital substance in the cerebrospinal fluid might be low at the same time that the concentration in the blood and lymph is essentially normal, such studies will have to be included in the orthomolecular approach to treatment of mental illnesses.

Pauling is carrying on some studies along those lines. The scientific world as indeed all the world is waiting anxiously to receive some of the results from this great scientist.

L.H.N.

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New Standards In Malpractice Cases

It is now time to take a closer look at the present means of disposing of malpractice cases. This has become mandatory since the "locality rule" which has been followed for many years is virtually fallen. The locality rule has been one of the most important bases of the legal standard to which a physician is held when his medical conduct is to be judged in a court of law. This standard has traditionally been that the physician must act as another prudent physician practicing in the same community would have acted under the same circumstances. To make this rule functional it is required that other physicians in the same locality be available to testify either that the practice under question was prudent in this community or that it was not. The basic issue then was for a lawyer to be able to obtain expert medical witnesses in a community to testify against a colleague, an admittedly difficult assignment.

The lawyers finding themselves with unavailable expert testimony succeeded in having statutes passed allowing text-books as evidence in lieu of expert testimony. This apparently was not enough and direct assaults upon the "locality rule" was sure to follow as indeed it has. Thus far the most common change has been to adopt a "similar community" instead of the traditional same community concept—that is if one could prove to a judge's satisfaction that two cities even though they were in different states had comparable standards of medical practice it would then be possible for physicians of one city to testify in an action involving a physician in the other.

In another assault on the "locality rule"[1] a Louisiana court held that the "same community rule must fall if the standards in that given community are below what the court deemed a reasonable minimum standard." In that case a woman was severely injured when she fainted before an X-ray examination because of a pre-existing condition that would have been discovered if a routine history had been taken by the radiologist. The hospital raised the defense that it is not the standard in the community or even surrounding communities for a history to be taken in the X-ray room. The court, however, held that the standards of the entire community are too low and must be raised accordingly. The court obviously missed the mark in assessing the realities of hospital practice. Nevertheless there emerged the concept of an unacceptable standard, a very important concept indeed.

The same rejection of the "locality rule" occurred recently in Massachusetts.[2] It involved an anesthesiologist practicing in a New Bedford hospital. During the course of a delivery the anesthetist administered a spinal anesthetic containing 8 mg. of pontocaine in 1 ml. of 10 per cent solution of glucose. When the patient attempted to get out of bed later she slipped and fell on the floor and subsequently even up to the time of trial complained of numbness and weakness in her left leg. Testimony was given by eight physicians and in the words of the court "there was ample evidence that the condition did result from excessive use of pontocaine" and that good medical practice required a dosage of 5 mg. or less. The defense, however, also presented evidence that the customary dosage in New Bedford in such a case was the larger amount, 8 mg.

At the trial the judge instructed the jury concerning the law of Massachusetts before this case. "The defendent must measure up to the standard of professional care and skill customarily possessed by others in his profession in the community which is New Bedford and its environment . . . if in the case it were determined by a jury that the ability and skill of a physician in New Bedford were 50 per cent inferior to that which existed in Boston a defendent in New Bedford would be required to measure up to the standard of skill and competence and ability that is ordinarily possessed by physicians in New Bedford."

The Supreme Judicial Court, however, reversed the lower court verdict for the defendent physician and sent the case back to for a new trial stating that "the time has come when the medical profession should no longer be Balkanized by the application of varying geographic standards in malpractice cases," and that the general practitioner or specialist should be held to the standard of skill of the average general practitioner or average member of the profession practicing the specialty "taking into account the advances of the profession." The court accepted the fact that the medical resources available to the physician are circumstances that must be taken into account to determine the skill and care required, but it is quite clear that the advances of the profession as a whole will be the determining factor in the future.

The fact that the Massachusetts court has abolished the "locality rule" and substituted a standard that is truly national in scope is quite significant. It requires all of us to take a close look at the deeper issues inherent in this and similar decisions. Why has the locality rule fallen? What has brought about the emergence of doctrine of "res ipsa loquitur" and common knowledge that allowed a jury to decide certain issues without the need for expert opinion evidence?

Some say that it is due to "the chronic refusal of physicians to come forward and testify against a colleague in a case that clearly merits such testimony." But this can hardly be the case since physicians found by their colleagues to have been responsible for an injury to a patient always advise him to settle the case. Furthermore, both the Louisiana and Massachusetts decisions were not based upon any complaints about inability to marshal medical testimony against the defendent physician. The decisions seem more to have been motivated by public pressure for the highest standard of medical practice from each general practitioner and each specialist.

It is hoped that the medical resources available in the local community will continue to play an important part in future decisions although it is clear that in an increasing number of jurisdictions, this will no longer hold. It is now time to look to a better means of disposing of malpractice cases.

L.H.N.

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Medical And Ethical Aspects Of Kidney Transplantation

When kidney function has failed, then treatment by dialysis is effective. However, it is extremely expensive and there are not sufficient facilities for all who need it. The first ethical difficulty arises in deciding who should be treated and who excluded. Alternatively a healthy kidney can be transplanted to replace the diseased one. If the kidney is removed from a live, healthy individual for the benefit of a sick one, even more serious problems may arise. The healthy donor cannot himself possibly benefit and yet has to face risks which may threaten his own life, when there is no certainty that the transplant will succeed and in the end his sacrifice may be in vain.

The donor also faces unpredictable later risks which may in the long run shorten his own life for the remaining good kidney can become affected by disease or in injury as McGowan reports in one of his cases.[1] It may also be difficult to discover whether the donor is truly willing to give a kidney since he may be subjected to hidden pressures amounting to moral blackmail from other members of the family to force him to "volunteer" to give a kidney. McGowan also documents just such an experience of pressure on a father to donate a kidney. Fortunately a cadaveric kidney became available and the patient recovered.

Frequently no family donors are available and then dependence must be on unrelated donors biologically, such as a spouse or a volunteer from a prison. In the first instance such donors may have strong motivation for offering a kidney from their close emotional bonds but their children need to be considered also. It would seem wrong to jeopardize the life of a second parent without any certainty that the transplant will be successful. In the second instance Starzl[2] now feels he made a mistake in accepting prison volunteers and his experienced view in this matter is worthy of respect.

A final argument against the use of unrelated live donors is that the results are no better than those obtained from the use of cadaver kidneys. Original results from the use of cadaver kidneys were not as good as those from live donors for a variety of reasons. The situation now is quite different. Kincaid-Smith et al[3] have applied themselves to the solution of special problems associated with use of cadaver kidney. They have reported 71-78 per cent successes, the deaths having occured in the first six week after grafting. This suggests that with proper preparation there may actually be no superiority of a related donor kidney over a cadaveric kidney.

There are encouraging reports that the life of a kidney outside the body may be prolonged considerably by preservation with hypothermic perfusion and use of a membrane oxygenator.[4] Extension of the extracorporeal life of the kidney even to twenty-four hours would be adequate for tissue typing as well as preparation of the recipient and mobilization of the transplant team. Without elaborate methods of kidney preservation it is still possible to achieve a sort of tissue typing by preliminary typing of the recipients. If they are found to lack most or all of the antigens considered important in transplants such patients would be difficult to match and better managed by intermittent dialysis. It is astonishing that so many patients all over the world survive with good kidney function after receiving cadaveric kidneys when the only form of matching used was major blood group compatibility. McGowan cites seven such cases of whom six survived.

Good preparation of patients with a period of dialysis sufficient to restore a nearly normal nutritional and biochemical state probably has contributed greatly to the considerable improvement in transplantation statistics. Increased experience has also helped to reduce technical surgical failures especially with regard to the ureter. Increased experience with immunosuppressive therapy has also contributed and further improvement can be hoped for from the use of anti-lymphocyte and anti-thymic sera. Tissue typing methods may also help by reducing the strength of the incompatibility barrier thus permitting the use of lesser amounts of less toxic methods of immunosuppression. However, with 80 per cent success already achieved[5] by random matching of cadaveric kidneys the best the tissue typing technics can achieve is 20 per cent more improvement and this is still worthwhile.

The successful kidney transplant program depends on association with a well organized dialysis service which can make and keep patients fit until an opportunity for transplant occurs. Some of the past failures can now be attributed to the fact that they were carried out as an emergency on an unfit patient. If a patient is in terminal renal failure, he is unfit for transplant and requires dialysis to make him fit for the operation. Once he becomes fit then transplantation can be carried out any time thereafter that is convenient.

Some transplants will fail but failures are becoming fewer and failures if recognized early and the kidney removed should not result in death of the patient. The dialysis program should be able to accept these patients again and keep them fit until another kidney can be obtained.

Some of the original ethical problems are vanishing as increased success is achieved with cadaveric transplants. With such successes it would be unethical to consider using a kidney from a live young donor especially from a woman in the reproductive period of life. There may still be rare circumstances in which a kidney from a parent could reasonably be used especially if the parent is old enough not to have responsibility for a young family. The high incidence of success from transplanting a cadaveric kidney has made completely unjustified the use of a kidney from an unrelated live donor which offers no greater likelihood of success. As technology marches on the ethical problems in kidney transplantation are rapidly disappearing.

L.H.N.

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Cancer Trials: I. Immunologically Competent Cells In The Treatment Of Malignant Disease

There is much evidence that the body defense against malignant neoplasm is mediated through lymphocytes rather than by circulating antibody production. When the host's defenses fail, further widespread metastases will develop. In mice bearing subcutaneous transplants of a mammary carcinoma, growth of the tissues could be significantly retarded by sublethal whole body radiation and intravenous injection of spleen cells from a strain of mice that had been immunized against the tumor. A logical consequence of such an experiment was to treat patients with malignant disease by the injection of non-immunized allogeneic spleen cells. The results in a small series of patients showed that tumors could indeed regress with this form of treatment.

The greatest difficulty in testing the treatment of malignant disease with allogeneic spleen cells has been to have viable spleen cells available and a suitable patient available at the same time. To overcome this difficulty it was necessary to have available spleen cells at all times and this could only be achieved by a successful method of spleen cell preservation. Previously Symes et al[1] have shown that human spleen cells can be stored as a cell suspension at −196° C. for at least 50 days with no loss in the viability of the individual cells. They assessed the viability by the cells ability to undergo "transformation" during culture in the presence of phytohemagglutinins after storage, and also by the incorporation of tritiated thymidine with the cells at various intervals after the start of the culture. This indicates the cells have retained their ability to grow and reproduce.

Symes[2] has now extended the technic of storage of all cells obtained from a human spleen which had been removed for therapeutic reasons, generally during an operation for cancer in the esophagogastric region. This enabled them to establish a human-spleen-cell bank. Satisfactory viability of the stored cells in the presence of dimethylsulfoxide was found for seven out of nine spleens, the largest period of storage was 227 days. One spleen had cells with an especially low transformation rate and was found to contain a metastasis from a malignant melanoma. If this is the reason for the poor transformation rate, then cultures of cells from the spleen which has been removed in the course of treatment for malignant disease may afford some guide as to prognosis. This opens up a matter worthy of further investigation.

It is now apparent that a spleen cell bank has several uses. First of all it can be a source of cells for hematopoietic replacement after chemotherapy with cytotoxic drugs or radiotherapy. Second it can be a source of antigen in the production of heterologous human antileucocyte serum. Thirdly it can serve as a source of immunologically competent cells for use in the treatment of malignant disease.

Stored spleen cells have now been used to treat 5 patients in the terminal stages of malignant disease.[2] The treatment at first was to give an antisuppressive drug followed 48 hours later by an intravenous infusion of an allogeneic spleen cell suspension. All patients eventually died from progress of their disease but in three of those receiving allogeneic cells, a regression was noted of 4-6 weeks duration. Because of this unsatisfactory result, the authors have now explored the use of lymphocytes from different species (zenogeneic) which have been sensitized to the tumor. Two patients who were given pig spleen cells sensitized to the tumor showed striking evidence of tumor necrosis. Further evaluation of this therapy obviously is warranted.

These patients had malignant melanomas. One difficulty in assessing therapy in such patients is that progression of the disease may be episodic and such progression may be followed by periods of temporary regression. Although the eventual outcome with zenogeneic cells was again disappointing, the immediate results were more encouraging than were those obtained with allogeneic cells. It was surprising to see how well the injection of zenogeneic cells was tolerated and this is encouraging to permit an increase in the total dose of cells in future patients. Both patients in whom this was tried had widespread and multiple lesions and it seemed quite certain that only some of the lesions were attacked by the immunized lymphocytes.

Since we know that there exists tissue immunity against cancer[3] efforts directed towards the utilization of the immune mechanism in the treatment of cancer is well warrented and we look forward with hope to the improvement in this method.

L.H.N.

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Amino Acid Dependent Cancers: L-Asparagine In Leukemia

The proof that hormones can influence cancer is now well established.[1] One can achieve a cycle of growth and atrophy of the prostate by providing or withdrawing testosterone. In the absence of testosterone the prostatic cell shrivels but does not die. The prostatic cancer cell is entirely different. It grows in the presence of supporting hormones but it dies in their absence. Thus it can be stated that some cancers are hormone dependent and these cells will die when their supporting hormones are eliminated. Now we have proof that some cancers are dependent for their survival on the existence of an essential amino acid L-asparagine.

It had been known for a long time that cancers are rare in guinea pigs and it turned out that guinea pig serum inhibited certain mouse and rat lymphomas. The substance in the serum which was responsible for this remarkable action was found to be an enzyme L-asparaginase. The inhibiting effect of this enzyme does not involve any immune response but is a direct one. It developed that the cells of the sensitive tumors including lymphosarcoma in the dog and various transplanted rat tumors including carcinosarcoma[2] are dependent on an external source of the amino acid L-asparagine while other insensitive cells can do very well without it.

When L-asparaginase containing fractions of guinea pig serum was administered to a child suffering with acute lymphoblastic leukemia, it caused a fall in the white cell count and a shrinkage of the enlarged organs. Others have confirmed those findings and also noted a complete temporary remission. Since L-asparaginase does not affect normal cells, it could be a valuable means of treating cancers whose cells are dependent for their maintenance on L-asparagine. Oettgen et al[3] in fact demonstrated that L-asparaginase will induce remissions in some cases of acute lymphoblastic and acute myeloblastic leukemia and they observed a positive correlation between the in-vivo response and the demonstrable in-vitro requirement by the leukemia cells for L-asparagine. This opened the way to determine those patients who are likely to respond to L-asparaginase treatment. Such patients can be

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picked out by a single laboratory test. Because of the present extreme rarity of L-asparaginase, the simple determination of the sensitive tumors is obviously an extreme advantage.

At present two sources of anzyme exist; the guinea pig serum and Escherichia coli which produces two L-asparaginases only one of which is effective against sensitive leukemias. Escherichia coli was the source of the enzyme used by Oettgen and his colleagues but unfortunately the preparations were not entirely pure and intravenous administration was followed by chills, fever, nausea and vomiting. Side-effects were also observed in patients with insensitive tumors so that the symptoms cannot be attributed to destruction of the leukemic cells. The reasonable conclusion was that the side-effects were probably produced by residual bacterial products.

No other toxic effects have appeared either from the enzyme itself or from the aspartic acid generated from the destroyed asparagine. However, what was noted was that some patients developed sensitization to the preparation and it was not clear whether this was due to the enzyme itself or to other bacterial products in the preparation administered. The present situation is similar to what we experienced in the early days of penicillin therapy. We have a biologically produced impure agent, procurable only in small amounts at great cost. It seems highly potent against certain sensitive cancers although the best dosage and methods of administration have yet to be worked out.

Nevertheless the hope is that L-asparaginase may turn out to be a unique chemotherapeutic agent against cancer, effective because of a specific metabolic defect in certain cancer cells. Implicit in this story about asparagine is that other cancers may also be dependent upon some as yet unknown nutrilite and thus a new vista is opened in our search for the cure of cancer.

L.H.N.

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Requirements For A Normal Offspring

The egg like the sperm is intolerant of abnormal delays. There have been many observations in a wide variety of animals on the effects of such delays on both mortality and defective growth or development among the offspring. From studies of marine invertebrates on to frogs and mammals the story is the same, the egg is intolerant of abnormal delays.[1 7] Information of recent years in the various chromosomal aberrations in man has brought another aspect of the aged ova to light that of preovulatory aging of the egg. The number of eggs in mammals is thought to reach its maximum in embryonic or in early post-natal life after which no new eggs are formed. In man oogenesis is believed to cease at the time of birth.

The maximum complement in man has been estimated at about 5 X 10.^{6}. Of these no more than 500 mature and are ovulated during reproductive life. The remainder degenerate at various times in life. A large number are said to be lost at puberty. During normal development the eggs enter the first meiotic division at about the time of birth, remain arrested at this stage until shortly before ovulation. This resting phase for ova may extend for forty years or more in man and allow for preovulatory aging.[2] This may account for the increased incidence of mongolism (Down's Syndrome) towards the end of the reproductive life. The incidence in the whole population is about 3 per 2,000 births. In women over age forty-five the incidence rises to one in forty.

Increased maternal age may have other harmful effects on the developing embryo. Milham and Gittelsohn[3] have shown that congenital effects not associated with recognized chromosomal aberrations were also dependent on maternal age. These included spina bifida, microcephaly, cleft lip or palate and clubfoot and even more striking evidence associating congenital heart defects and hydrocephalus with maternal age. In such cases maternal age may act through different mechanisms not dependent on aging of the egg but reflecting a less favorable uterine environment in the older female. The reproductive efficiency of mammals thus appears to wane as the animal approaches the end of its reproductive life and one manifestation of this is an increased rate of abortion. Delays of egg ripening can be brought about by pentobarbital and this can lead to developmental irregularities (in the rat).[4]

There are now recognized some delays in the ripening of the egg produced experimentally which seem not to affect the health of the offspring. An increasingly common practice of this type is a new animal breeding practice known as synchronization which is in present use for cattle and sheep. Sheep

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ovulate spontaneously every sixteen to eighteen days. There is a practical advantage in having all sheep in a given herd come into heat together and lamb at about the same time. This is done by giving an oral progestational agent for a period of one cycle. Heat and ovulation are inhibited and on withdrawal all animals usually ovulate within three to four days. There are no reports of either embryonic or post-natal defects among offspring born after such delays. Perhaps this has some relevance to the use of the "pill" by humans.

Post-ovulatory delays in fertilization is rapidly fatal to the egg in most mammals. This is true in the rabbit, doe, guinea pig, rat, although the time of delay varies somewhat with the species studied.[5] Observations on man have been made between a single coitus and the time of the ovulatory rise in basal temperature. Marshall[6] in a study of 5,013 cycles found that if coitus was confined to the period after three daily temperatures of the higher level no conception occurred. Ovulation is believed usually to occur before the temperature rise and the fertilizable period for the egg in man therefore appears to be about three days. There is thus far however no valid evidence that eggs fertilized towards the end of this period give rise to defective offspring.[1] It is not encountered among couples practicing the rhythm method of contraception. Lanman, however, thinks the potential hazard of delayed fertilization remains important particularly in man in whom sexual behavior affords no assurance of the freshness of the egg at the time of fertilization nor the sperm for that matter.

Post-ovulatory delay in fertilization may lead to polyspermy—the penetrance of the ovum by more than one sperm.[8] In some animals even if this occurs only one sperm will unite with the nucleus of the ovum and the remainder will degenerate. In many animals immediate penetration of the egg by a sperm rapidly alters the membrane producing a block to prevent polyspermy in all but a low percentage of fertilized eggs. Of course, when a mammalian ovum is fertilized by more than one sperm abnormal development and early death of embryo usually results.

In nature we find some mechanisms to prevent post-ovulatory delay in fertilization. Some mammals will accept the male only during periods of heat which are closely related to the time of ovulation. Others like the rabbit ovulate in response to coitus. In either case the ovulated egg is protected against a delay in fertilization. Neither of these mechanisms

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is operative in the human being in whom mating occurs without reference to the time of ovulation.

It becomes clear that the normal offspring may be expected when the egg is fresh, the sperm not aged and the uterine environment is favorable.

L.H.N.

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Undesirable Trends In Personal Medical Care

We all realize the importance of direct and personal attention that is given by the doctor to his patient. Illness will always remain an intensely personal thing. No one knows this better than the physician when he himself becomes a patient. This precept of direct and personal relationship between the patient and his doctor appears to be disintegrating under a number of identifiable pressures some perhaps reducible while others are probably not.

The heaviest pressure is that of time. The shrinking supply of this commodity is owing to a number of factors. One is his enlarging patient load, resulting on the one hand from a more rapid increase in population relative to the increase in the number of physicians. Another is the phenomenal increase of scientific advances and the new available treatment for illnesses previously not amenable to medical intervention. Another is the mounting burden of paper-work incident to the rise in third-party participation in the economics of medical care on the part of the private and especially governmental health agencies. In addition even in many community hospitals a considerable amount of time of the attending staff must be given to devising and carrying out approved interne and resident teaching programs without which in today's shortage of house-officers the hospital wallows hopelessly in a buyer's market.

The accelerating growth of knowledge and technology has led in many places to the Chief's feeling obliged to spend more ward round hours in the conference room discussing such matters with residents and students than are spent with patients who as a result may receive no more than a "head in the door" and a perfunctory question or two. Then there is overwhelming increase in medical literature and who has the time to keep his chin above water in the towering wave of new information. It is almost inevitable that these and other events, conditions and activities will occupy more of the doctors precious hours as the years or, at the present rate, months go by.

With the shortage of house-staff in many communities and the declining number of generalists, and at the same time development of intensive care units and coronary care units in these same communities, the internist is becoming implicated in the emergency care of the patient. He needs to interest himself in mouth to mouth resuscitation, external cardiac massage, electrical cardioversion in order to utilize these newer modalities. He needs to teach these procedures to house-staff nurses, firemen, policemen and ambulance drivers and truck drivers. Soon he will need to teach recognition of a possible coronary attack. Now with telemetering of ECG's the internist becomes further involved and his time for personal care of the patient shrinks still further.

These time robbers of personal attention it appears are likely to be reinforced by new developments now looming on the horizon. There is the increasing tendency on the part of certifying specialty boards, and residency review committees with the enthusiastic support of the young medical graduate to require residents and internes be given major or even "primary" responsibility for the hospital care of the patient. It may be highly desirable from the standpoint of the trainee and it may be good for him if he has adequate supervision. But what happens here to the personal care of the patient by his responsible physician. In fact it is badly shaken and not infrequently the patient is confused and wants to know who his doctor really is?

One response to the shrinking time of the physician is the emergence of belt-line methods of laboratory or even "clinical" study of patients conducted by auxiliary medical personnel being employed in some prepayment centers replacing in certain respects what used to be the functions of the physician himself. The question remains whether this will give him more time with his patients or merely allow him to see more patients with the present minimum of minutes allotted to each. Will he be running faster to stay in the same place?

He may, however, be aided by the revolutionary and pretty certainly prophetic plan now in operation at Mount Sinai, to educate and train physicians, assistants, nurse associates and the like who can do many of the things presently done by the master even including physical examinations leaving the genuine article to the conventional M.D. to draw conclusions, make final decisions and give advice with only the minimal "laying of hands." This is the doctor depersonalized, deleted, and distant. In fact he may even become more so with the general adoption of the diagnostic computer and the development of the team concept of medical care.

We as physicians must face up to these new trends in medical practice. It will probably not be possible perhaps in the long run even not desirable to stem the tide of these trends. One thing is certain, the patient will not adapt easily to this kind of care even though he must accept it. Illness is an intensely personal thing as the physician learns when he himself becomes a patient.

L.H.N.

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Physical And Biological Influences In Traffic Accidents

The traffic toll on our highways is immense. Accidents appear to be primarily an affliction of youth and early maturity. This fact is based upon the inexperience and also on temperaments and attitudes characteristic of youth and early maturity. Of the 53,000 killed on our highways in 1967 approximately half may be expected to be between 15-30 years of age. One motor vehicle death in five will involve a male, 15-24 years of age. One pedestrian death in four will involve a male, 65 years of age or older. It all adds up to a loss of 1,750,000 years lost prematurely. Loss from cancer and heart disease are not often lost prematurely. In this regard then motor vehicle accidents are far worse than cancer or heart disease.

It has become apparent that accidental injuries can be analyzed by the standard methods used to study the incidence and causes of disease, because accidents exhibit some of the same biological and physical interrelations as pathologic processes do. An epidemiologic approach to accidents thus would involve a study of the many influences including all aspects of the host, agent and environment and their interrelations. As in the pathogenesis of disease the necessary ingredients are a susceptible host, a predisposing environment and an exciting agent. Thus data concerned with the distribution of accidents are now studied in terms of who had them, when and where they occurred, different classes of injuries or agents and the mechanism of the injury.

In industry and the home the common responsible factors can be identified and controlled as for example machine tool guarding. For this reason the greatest advances in the control of accidents have taken place in these areas and accordingly the accident rates have shown a steady improvement through the years. The situations are stable, the environment settings are repetitive and there are repeated similar exposures. The great majority of highway and non occupational accidents by contrast are not homogeneous and usually involve nonspecific causes. In spite of these difficulties it is now possible to state some of the findings from an epidemiologic point of view and this may lead to measures for accident prevention.

The first thing that showed up in McFarland's studies[1] is that trained drivers especially those that had received formal instruction as beginners, tend to have fewer accidents. This means that the initial licensing should involve some formal driver training. A second point of great importance not as yet fully documented is proneness to injury. Drivers manifesting a poor adjustment to the social and personal demands of life do have a higher incidence of accidents. Even without access to accident records, accident repeaters as well as accident-free drivers can be identified by their history among such agencies as courts, credit organizations, social welfare agencies and public health and venereal disease clinics.[1]

Recent estimates of the role of alcohol as a causal factor have been revised upward to over 50 per cent of the fatal accidents.[2] There is substantial evidence that alcoholics despite their relatively small numbers in the population (not the social drinker) account for more than half of the alcohol related accidents. The incidence rises steeply as the blood alcohol level rises beyond .04 per cent. In Great Britain the law makes it an offense if one drives with an alcohol level of .08, and the driver loses his license for a year and receives heavy fines or imprisonment. In this country the law has yet to keep pace with scientific knowledge in this regard.

If alcohol is excluded then the extent to which advanced illness is a causative factor in motor vehicle injuries and fatalities has not yet been determined. We know that undiagnosed or untreated diabetes, epilepsy or some forms of cardiac disease such as coronary insufficiency or arrhythmias are potentially a hazard on the highway because of unexpected impairment of consciousness. However, after successful treatment many patients become safe drivers. The moral of course is go to your doctor to become and keep fit.

Older people, however, may have significant nonremediable conditions such as retinal deterioration that severely compromises their vision or impaired central nervous system function. In this regard it is well to remember that illumination decreases strikingly with increasing age in some patients and this is heightened by the tinted windshield. At sitting eye-level the tint will reduce transmission of light or ability to see outside by over 25 per cent. In general adequate criteria for disqualification have not been worked out by the medical profession for the licensing authorities. For example how poor does one's vision have to be for disqualification? How old does one have to be so that reaction time is too slow and the patient becomes confused? Obviously the physician must use his best judgment and advise his patient or licensing authorities that persons who might offer such a hazard should give up driving in the public interest.

There are many important temporary host conditions that affect accidents. Driver asleep accidents are very common. The disorganization of skills with fatigue or emotional states have been studied by McFarland and his colleagues. The influence of drugs and that of medications are obviously important contributing factors, simply and in combination with other agents. For example a combination of anti-histamines or tranquillizers with several drinks of alcohol can gravely impair conscious altertness in drivers and can sometimes be lethal as emphasized in World Health organization reports.[3]

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modern system of highways and throughways has resulted in fewer accidents but they are more often serious because they occur at higher speeds and the "overload" or complexity is greater for inexperienced, old, sick or drug afflicted drivers. Accordingly the accident-potential situation may build up more rapidly. Thus adverse road conditions, poor driving practices such as driving too closely, driving beyond the range of field of vision or error in passing another car give rise to many serious accidents.

Then there is the question of low level of illumination when combined with defective vision as causative factors since about two-thirds of the fatal accidents occur at twilight or at night. Defective vision need not be caused solely by retinal disease or by failure to wear glasses that correct for distance. It can be due to carbon monoxide from automobile exhaust or inhaled cigarette smoke[4] as well as the histotoxic effects of alcohol and certain drugs that impair the transport or delivery of oxygen to the cerebral or retinal tissues or its utilization there. Many persons use nitrates over long periods and collect significant amounts of methemoglobin. It is said that the smoker who consumes two packages of cigarettes in one day is living in a rarified oxygen atmosphere equivalent to 8,000 feet altitude.

The final result of all these physical and biological influences is poor performance and a greater liability of a fatal crash. An epidemiologic analysis of the causes of accidents on the highways has been and will continue to be of great importance in reducing one great scourge of our modern way of life, traffic accidents.

L.H.N.

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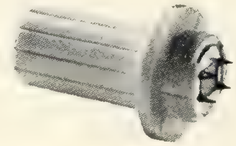

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The
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Melvin Lewis, M.D., Guest Editor

The Yale Child Study Center, while still housed for the most part in the building that arose from the artist's drawing depicted on the front cover, has grown and developed since its inception in 1948. This two-part symposium is in part a testimony to this growth, reflecting as it does a part of the wide range of interests and endeavors of its faculty. It is fitting, therefore, that the Child Study Center's Director, Dr. Albert J. Solnit, Professor of Pediatrics and Psychiatry, should introduce this second part of the Symposium with a brief description of the concepts that have been a guiding force in the work of the Child Study Center.

The Conceptual Basis of the Child Study Center, Yale University

Albert J. Solnit, M.D.

Over a year ago the Editor invited the staff of the Yale Child Study Center to prepare scientific papers that would illuminate the many facets of our knowledge about psychological aspects of child development and child health for the readers of this journal. Under the able editorship of Dr. Melvin Lewis, a senior staff member of the Child Study Center, a wide array of papers has been presented in the June and August 1968 issues of *Connecticut Medicine.*

The Yale Child Study Center, since its inception in 1948, has developed its services based on the assumption that training and research programs should be anchored in clinical services that are relevant to the communities it serves. The Center consists of four sections: child psychiatry, child development, child psychology and the nursery school. As Dr. Senn, its first director, indicated in his historical perspective, this institution was organized in order that several disciplines concerned with child life could work together to meet the needs of children and their families in our society, at the same time as this Center served the aims of the University to acquire and impart knowledge about children and childhood.

As the Center prepares for the next decade, we plan to retain essential strength in the Center's primary fields (child psychiatry, child development, child psychology and early child education) as well as to continue close collaboration with the Departments of Pediatrics, Psychiatry and Psychology and with the Law School. At the same time, there are plans to enlarge the Center's commitments in three crucial areas:

1. The longitudinal study of children from poor and disorganized families and their earliest developmental characteristics from birth to the age of seven. This study, organized by Dr. Sally Provence, who directs the Child Development Unit, concerns itself with knowledge about the plight of the large group of children who grow up in disorganized families, foster homes or institutions. The action-study will investigate how the permanent intellectual and emotional damage suffered by these children can be prevented by appropriate and sustained interventions.

2. An experimental psychological study of social and cognitive functioning in prekindergarten schools for the children of the poor. This study, organized by Dr. Edward Zigler, who directs the

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DR. ALBERT J. SOLNIT, Director, Child Study Center and Professor of Pediatrics and Psychiatry, Yale University School of Medicine.

Child Psychology Unit, will experimentally investigate modes of socializing and learning that will enable early child educators to adapt curriculum and educational techniques to meet the learning characteristics and deficits of these disadvantaged children.

3. The establishment and evaluation of new models of collaboration between clinicians and teachers in the public schools. Directed by Doctors Albert J. Solnit, A. Herbert Schwartz and James P. Comer, this demonstration study has evolved from a decade of collaborating with teachers, principals and administrators in public schools, especially prekindergarten through the sixth grade. Child psychiatrists, social workers and social scientists from the Yale Child Study Center are prepared to contribute in a sustained and systematic manner to the establishment of new models of education. In these models the knowledge and experiences of clinical specialists in child and family development can be integrated into and serve the primary educational aims of public school programs, especially those designed for environmentally disadvantaged children.

At the Yale Child Study Center, pediatricians, psychiatrists, psychoanalysts, psychologists, social workers, educators and social scientists collaborate in the study and care of children and their families as is indicated by each child's needs and condition. In this symposium some of the critical needs of normal and deviant children are considered and elucidated in practical as well as theoretical terms. We are grateful for this opportunity to serve *Connecticut Medicine* and its constituents.

Teaching Staffs In Medical Schools

Preparing competent practitioners, investigators and teachers for the future, so crucial to the national welfare, is the major obligation of the teaching staffs. Even with extensive physical facilities, large scholarship, traineeship and fellowship funds, a continuous stream of excellent medical students and abundant financial support for investigations, the recruitment and stable employment of competent medical faculties would still be the major responsibility of medicine for its own future. Unless the serious shortage of teaching personnel can be corrected soon it will make difficult the expansion of existing medical schools, the growth of postdoctoral medical education, the creation of new schools and the maintenance of an adequate supply of well qualified practitioners.—Rappleye, W. C.: Alan Gregg 1963 Lecture: Expanding Functions of Medical Education, *J. Med Educ 38*:899-905 (Nov) 1963.

ON PREDICTING MENTAL DEVELOPMENT

Sally Provence, M.D.

More than ever before in the medical care of young children, questions about normality and abnormality of mental development confront the physician. The public has become aware of mental retardation, birth defects and personality disorders. The debilitating effect of an impoverished or noxious environment upon growth and learning has also become rather generally acknowledged. Parents are both more knowledgeable about landmarks in development and more concerned about their meaning and the physician is often called upon to examine an infant or young child and to give an opinion not only about his current status, but whether he has the capacity for normal development. In some cases the physician will feel confident and in other cases uneasy when confronted with this task. Questions have been raised for many years in the fields of medicine and psychology concerning the accuracy of predictions made about the developmental potential of the infant or very young child and therefore about the wisdom of trying to make them. The issue is complex. The purpose of this essay is to call attention to the data most often used in making predictions and some of the conditions which influence predictability.

When there is some delay or deviation in the child's development the physician is faced with questions about its significance: is it a transient sign or an indicator of a biological defect? is it a variation that can be considered within the range of normal? does it suggest a serious outcome? should it be called to the attention of the parents or not? what can be said about its meaning for the future, e.g., what is the prediction? should a prediction—short or long term—be made at this time? Furthermore with the rapid increase in information about chromosomal characteristics, inborn errors of metabolism and other congenital and hereditary disorders, questions of what can and should be predicted in early infancy have become even more complex than before. In order to present an approach to these questions it is necessary first to briefly define the point of view. The development of the child is a dynamic, unfolding process, which is co-determined by inborn and experiential factors. Development and the learning which is an integral part of it come about through an interaction of in born, maturing systems and the forces of the environment. In the process of maturation both somatic and mental innate factors are called successively into play according to an inherent biological timetable. We are accustomed to considering innate constitutional factors in understanding the development of the body and its organ systems, but this concept is more inclusive than that. The infant's constitution also includes primitive forms of the mental equipment that serves perception, motility, thinking, memory and other abilities which help the individual gradually to perceive and deal with reality. It includes the psychic drives which have their own maturational phases. One of the needs of the infant is for an environment—that is for a variety of stimuli and experience—in which all of these maturing systems, somatic and psychic, can be organized into functional units and integrated with other functions and systems at successively higher levels.

In speaking of an infant's environment we refer in the beginning mainly to the quantity and quality of maternal care within which a very wide variety of sensorimotor, social and affective experiences occur. As he grows older his environment enlarges to include his father and other family members, the "things" that are part of the physical world and a rapidly growing variety of increasingly complex experiences that constitute his daily life. The crucial role of adequate nurturing and of other experiential factors in influencing the child's development has been amply documented.

We do not expect that the environment of any child is likely to be ideal, but we do know approximately the conditions and experiences that are necessary in order to meet his more crucial developmental needs. Assessment of the adequacy and appropriateness of his relationships to others and of the experiences which promote or impede development are an important part of any evaluation of the child.

How then do we approach the problem of predicting development? If an infant is developing well, we assume (i.e. predict) that he will continue to do so. For example, in respect to motor development if the infant creeps and pulls to stand at the expected time, we assume that he will walk and

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run similarly normally. If the pre-stages of speech are present, i.e., the social vocalization, the ability to make vowel and consonant sounds and later to combine them, we assume that speech will develop adequately. In making this prediction we are also assuming the influence of an environment in which at least the child's most important developmental needs are met. It is obvious that the accuracy of predictions lies in the fact that most infants are born with the potential for adequate development, and that many, though perhaps not most, are reared in environments that are reasonably good. It also takes into account that the normal early phases of the maturational process reflecting normal structural and biochemical processes are likely to be followed by similarly normal processes later, This kind of prediction is based upon probabilities, however, and it is important to note there are inborn disorders of development that become manifest not in early infancy but only later. We are also aware that probabilities help very little in the specific situation of a particular patient.

In his daily work when called upon to predict development the physician is concerned not so much with individuality, though this is interesting, nor with the many varieties of healthy personality development, learning and social adaptation, but with pathological processes. In predicting retarded or deviant development he relies on several different types of information in addition to his carefully taken history of health and development.

The appearance and physical characteristics of the child. Predictions about future mental development of the neonate who has the physical characteristics of mongolism, microcephaly, gargoylism, cranio-facial dysostosis and many other defects recognizable at birth or in the earliest months of life obviously are based upon accumulated knowledge about outcome in other children with similar physical traits. While in many instances this method is valid, we have learned that errors are not rare in the prediction of outcome for a specific child. Characteristically when a congenital disorder is newly discovered and two or six or ten cases with a known developmental outcome are described, we tend to assume that all children with these physical traits will be similarly affected. As experience accumulates, and the "exceptions" or more accurately the variations of the originally described picture become visible, we extend our conception and revise our predictions. Mongolism, which has been recognized for many years is a case in point. Children were formerly called mongolian idiots and were assumed to be remarkably uniform in mental capacity and personality. Later experience has shown that there is a rather wide variation in the eventual level of intellectual ability.

The physician also relies upon—

The results of laboratory examinations. Of the many examples available, only a few will be cited.

Disturbances in amino acid metabolism, carbohydrate metabolism, endocrine metabolism and pigment metabolism are being continuously explored since biochemical genetics has provided an approach to understanding them. Advances in biochemical methods make it possible to correlate more closely the effects of disordered metabolism upon general development. Textbooks and articles which purport to give firm answers about what can be predicted are likely to be out of date before they are disseminated. It is already recognized, for example, that there is no one predictable developmental outcome for infants with phenylketonuria, congenital hypothyroidism or galactosemia. Long range predictions about metal development for an individual child should be made only with the greatest caution in many of these disorders and probably only after a period of observation during which sequential developmental assessments are done.

The examination of chromosomal material is another burgeoning field and as more experience is accumulated and techniques improve there are variants in chromosomal structure whose relevance for later development will not be adequately understood until children can be followed over a period of years. We are now familiar mainly with the most serious clinical pictures in which chromosomal abnormalities have been identified. We are now in a period during which more information is available about chromosomal characteristics than we know how to use clinically.

Developmental and psychological tests.

The third major source of information used in predicting development has been derived from the clinical developmental and psychological tests.

The most widely used infant tests of development were worked out in this country in the late 1920's and early 1930's mainly by Gesell, Bayley and Cattell in this country, and Buehler in Vienna. They were considered as downward extensions of such tests of intelligence as the Binet and appeared at a time when intelligence was thought of as being fixed at birth. There was an understandable burst of enthusiasm for the tests since they made possible a systematic set of observations said to be "normative" from which a score could be obtained. This score, called a developmental quotient or in some tests an intelligence quotient, was often used clinically to predict future intelligence. The situations in which these predictions proved incorrect were as frequent as those in which they were correct and there has been for many years now an almost continuous controversy regarding the predictive value of tests done during infancy.

It is not relevant to this paper to go into the evidence presented on each side of this controversy. Developmental tests, like other tests the clinician uses, have very significant values and limitations and are valid only if administered by persons who are aware of what they can and cannot tell. In many instances they can be used to predict future mental development and in some instances personality traits. Moreover, much can be said from these tests about the functional integrity of the central nervous system.

The significant question is not the old one, "do infant tests have predictive value?" but should be posed as follows: under what conditions and in regard to what developmental disorders can the scores on infant tests be closely correlated with scores obtained on tests of intelligence at later ages? Posed in this way the question can be examined more relevantly. In general it can be said that early and later scores on tests correlate most closely when a "non-correctable," recognizable inborn biological defect is involved. Syndromes such as mongolism or primary microcephaly are examples. When a correctable or at least treatable disorder is involved such as phenylketonuria or cretinism, test scores may change markedly over time, depending upon the timing of treatment and extent to which correction of the metabolic or endocrine defect is possible.

The situation differs again when circumnatal insults to the central nervous system from such problems as hypoxia at birth or hemolytic disease of the newborn damage a brain which heretofore has developed normally. Even in the presence of damage, the child may be endowed with a strong thrust toward normal development. Obviously, outcome will be related to the extent and location of the damage. If, as many do, the infant has motor tract involvement which is one of the common visible abnormalities, and one tries to predict future mental development from a test which contains many items dependent upon motor ability, a prediction of future intelligence is a silly exercise. The experienced child development specialist will not expect that a D.Q. of 60 in such a child can be projected forward in time to an I.Q. score of 60 at age 5, or 6, or 10 years.

Another set of factors must be considered when environmental conditions have resulted in the infant's experiencing deprivation or trauma such as often occurs in institutional settings and in families in which parents are unable to nurture their children adequately. There are many reports, both from clinical and research sources, of the detrimental effect on the child's development of such life experiences. A developmental test done during the early years and at a time when the child is still in or fresh from such an experience assesses his condition at that point in time and is one of the most valuable means of identifying the way in which, and the degree to which his development has been impeded. Obviously, however, the outcome for the child depends upon how his development can be facilitated through improving his situation by whatever aids are indicated. The beneficial effect of improved care which addresses itself to his deficits and to his ongoing developmental needs is often quite dramatic. Residual effects of severe or long term deprivation and of traumatic experiences are, however, often visible in the child's personality development, in his physical growth and in the level and style of intellectual functioning. Thus in respect to adverse environmental conditions, as well as in some of the inborn metabolic errors, it may require several years in an improved situation and serial assessments in order to predict future development with some degree of confidence.

This brings up the last, and in a way the summarizing point, namely the necessity to view the question of predictability of development as a complex, multi-dimensional question rather than as a simple one.

Some of the experiences, both positive and negative, that children encounter in the process of growth are not predictable. Illnesses, accidents, educational and interpersonal experiences that facilitate development, or impede it are usually impossible to anticipate in a specific way for a specific child. If we accept the complexity of human behavior and of human experience it should not disturb us that we cannot provide extremely precise and categorical answers to more than a small percentage of the developmental problems. If we are reasonably well satisfied to make approximate or general predictions, the validity of predicting is much greater and usually sufficient to provide guidelines for the child's family in understanding and planning for a child with a developmental problem.

Prediction in Child Development Research.

The use of prediction as one of the valuable methodological tools in clinical child development research has come into greater prominence in recent years. In systematic, longitudinal studies of the developing child expectations about the course of various aspects of development (e.g., intellectual functioning, adaptive abilities, potential problems) emerge from the application of theory to knowledge about the current situation and the status and prehistory of the child. These can be stated as predictions of various types (short term, long term, general, specific, etc.) together with the reasons for the prediction. Experiential variables considered in the context of a specific child's individual environment and his phase of development can be linked predictively to possible specific effects upon development. The examination of outcome in children studied over a period of time makes possible the evaluation of the predictions with such questions as: did a particular prediction prove to be correct or incorrect and why? could a more accurate prediction have been made? what other data would be required to do so? what relevant influences could not have been predicted in this case? In addition to the advantages of studying the data and the conditions that allow correct predictions, incorrect predictions examined in this way have an established value in increasing our knowledge about normal and abnormal development which eventually become useful to the clinician.

In addition long term development studies and follow-up studies of children in whom it is possible to make a diagnosis of specific disorders in early infancy will continue to increase our knowledge.

In summary, predictions of mental development of the young child are reliable under certain conditions. The availability of a child development specialist who understands not only the techniques of assessment of mental development, but their predictive validity will be of assistance to the physician who is responsible for the care of the child.

PHS And Industry Mount New Attack On Air Pollution

Basic- and applied-research scientists may get a large share of the $10 million to be spent by the federal government and the oil and automobile industries over a 3-year period in a joint attack on the nation's air-pollution problems. The 25-30 different projects to be undertaken in a variety of basic and applied areas include: basic chemical interactions between fuels and vehicle exhaust emissions; development of test procedures for measuring pollutants; chemical studies of pollutants and their interaction and movements in the air; studies of the influence of pollutant on animals, plants and people; and the development of better equipment for analysis and control of pollutants. The program will be run by the Coordinating Research Council, Inc., of New York, with equal funds from the Public Health Service's National Center for Air Pollution Control, the Automobile Manufacturers' Assn. and the American Petroleum Institute.—*March 18, 1968 Scientific Research*

CONSIDERATIONS REGARDING THE THEORY OF AGGRESSIVE DRIVE DEVELOPMENT AND AGGRESSIVE BEHAVIOR IN CHILDHOOD

Melvin Lewis, M.D.

Introduction

Aggression today has come to connote, and be equated with, an act of hostility. This is unfortunate since we mean something different when we use the term aggression in its technical sense. Perhaps one should say that it is unfortunate that the noun aggression was used as a technical term in the first place just because it has indeed always had the general meaning of an offensive, or attacking, procedure. Yet even the dictionary[1] definition of the adjective aggressive provides us with alternative concepts: for example, "driving, forceful energy or initiative", "enterprising", "self-assertive", "obtrusive energy", as well as "combative readiness." The concept of an aggressive drive, like that of a sexual drive, is not a static one; rather, it implies a dynamic development. Indeed, values such as "good" or "bad" (or "healthy" and "pathological") ascribed to any particular aspect of aggressive behavior can be better understood in the context of that development.

Just as it is possible to conceptualize a progressive sequence of sexual development (Lewis 1968), so one can conceptualize a progressive sequence of aggressive development "aggression is a drive as innate, as natural, and as powerful as sex" (Storr 1968). And in considering that development, the same three considerations that comprise a definition of the sexual drive must be satisfied for any adequate comprehension of the aggressive drive; namely,

1) the source of the aggressive drive, which may be a state of body tension that makes a compelling demand upon the mind.
2) its changing aims, varying from direct, immediate discharge, to delayed, sublimated, or substitute gratification.
3) its changing object, that is the self or the person toward whom the drive is directed.

Furthermore, like truth, the development of the aggressive drive is rarely pure and never simple; it must also be considered in relation to, and interacting with, other complex, developing, psychic functions, such as memory, judgment, speech, object relations, defense mechanisms, and so on, as well as with the vicissitudes of sexual drive development.

Reflex Stage

Observations of young infants suggest that from the very moment of independent life the infant exercises certain rudimentary functions that in part serve to facilitate adaptation. Such functions may indeed be said to represent primary autonomous apparatuses (Hartman 1950). Perhaps it would be more correct to say that the adaptive aspect of these functions is rudimentary, since the functions themselves may be quite complex, and not rudimentary except insofar as they are manifest only during the earliest period of development. For example, such functions as the rooting reflex, the grasp reflex, the tonic neck reflex, and certain behavioral reactions such as anticipatory posturing and changes in activity that represent attention following an external stimulus, whether it be visual, auditory, or tactile: all these functions may operate in the service of adaptation and survival. The infant, in fact, is a sucking, looking, grasping, learning individual. In some cases the survival value of these functions is readily seen; in others it is less obvious. Anticipatory posturing and changes in attention states, reflected in changes of activity, clearly serve to alert the infant to his environment. In doing so they serve the adaptive and survival interests of the infant.

Each of these activities is enhanced by the infant's experiencing, to whatever extent this is possible in the infant, a measure of control over his environment. The measure of control is the extent to which the infant is able, say, to mentally assimilate the nipple, or the breast, or the mother, through the exercise of these functions. At the same time the environment—that is, the "ordinary devoted mother"—makes an adaptation to the infant and meets the infant's needs (Winnicott 1965). The infinite nuances of responses in the mother as she satisfies and stimulates the infant serve also to reinforce the child's ability to differentiate himself from

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[1] Webster, 1965.

his environment; that is, they facilitate the reality testing that is necessary to achieve further mastery of the environment.

Motor Stage

Such early functions appear to represent the anlage of what will soon become unmistakably the primary modality of adaptation in the infant's life; namely, motor activity. Indeed, reflex motor behavior can be viewed as the earliest manifestations of functions that will later be developed into complex forces available to the infant in his struggle to survive and adapt. Fortunately, adaptation is not entirely dependent on reflex motor behavior, at least in its most elementary forms. In any case, motor behavior itself undergoes a maturation (crawling, climbing, standing, walking, running, jumping; increased skills with hand, thumb and forefinger; coordinated balancing skills, etc.) so that more advanced motor skills continue to serve the purposes of adaptation. However, even the ability to sharpen and develop specific motor patterns would not be enough to ensure human development and adaptation, although it might suffice for an anthropoid ape.

Symbolic Stage

Rather, a uniquely human function begins to emerge in the form of symbolic representation. This symbolic function, later to be represented in part in the play and language development of the child, now begins to assume a significant role in the discharge and modulation of aggression. Put another way round, it may be said that the aggressive drive is both necessary for the formation of the symbolic process and is served by that process for modified discharge.

For example, by the age of two years, the infant's brain has matured sufficiently to allow him to articulate a few words. The environment to some extent stimulates, and to some extent necessitates, this further step in development, and the child's aggressive drive is mobilized to utilize this new maturational event of speech in the service of mastering that environment. Indeed, the first few words of the two year old are often expressions of this drive to master the environment. Thus the two year old might say "I want", or "give me", or "this!", or "I don't want to", or "no" (even when he means "yes").

Fusion of Aggressive and Sexual Drives

One may say that the child mobilizes his aggressive drive, or has his aggressive drive stimulated, at each new stage in maturation, in order to achieve a mastery of the newly emerging skill, and then to put it to work in the service of meeting the widening variety of needs the child is experiencing. It would be interesting, for example, but not possible within the present scope, to explore the line of development from the modified reflex behavior mentioned earlier to the degree of activity and aggressive drive required to achieve bowel control, and the ways in which bowel control serves to discharge aggressive drive tension and control the environment. Again, as the child develops, it would be interesting to examine the mobilization of the aggressive drive in the intrusive, inquisitive, invading curiosity of the child who is preoccupied with the anatomical differences between the sexes and how babies are made. Indeed, sexual and aggressive drive development become fused, and remain complementary to each other, except in certain pathological states when a de-fusion occurs (Freud 1927). Furthermore, a sexual aim may find expression in an aggressive act, just as aggression may be discharged in a sexual act (Hartman, H., Kris, E., and Loewenstein, R. M. 1949). Curiously, "sexual aggressions" during childhood were described by Freud before the concept of an aggressive drive was clearly formulated (Freud 1896).

Aggression in the Service of Development

Each maturing function elicited and motored by the aggressive drive achieves optimal development, and each subsequently serves to discharge in modified ways the aggressive energy of the child. For example, the cognitive operation of the child between 7 and 11 years of age has reached a stage in which mental actions are not only internalized but are also integrated with other mental actions to form general reversible systems, so that the child's thinking becomes reversible; i.e., he can not only say that $6 + 4 = 10$, but he can also say that $10 - 6 = 4$. Furthermore, the child is no longer dominated in his thinking by the configuration which he perceives at a given moment, but he can now take into account two variable at once. For example, he can take in height and width in judging the volume of water in a cylinder or a jar (Piaget 1950). This level of conceptual development is only possible after a long and complex development, starting with an active use of the body that involved the infant's aggressive drive. Further, this present capacity may be aggressively seized by the child in his zest for learning, and may in turn be used by the child in a variety of problem-solving activities as he deals with his widening environment. How rapidly the child advances in his subsequent cognitive development, and to what use this cognitive development is put, becomes to a large extent a matter of motivation, which in turn depends in part on the disposition of aggressive drive. Later, certain learning difficulties in children may be seen to arise from conflicts within the child around his aggressive fantasies at the time he would normally be putting these cognitive capacities to work in school.

The Aim of Aggressive Drive

In considering the theory of psychosexual development of the individual, there is little disagreement upon the end point, even though there may not be complete agreement about the earlier manifestations of infantile sexuality. The end point of sexuality in the stage of adulthood is approximately represented by an appropriate love relationship, sexual intercourse, orgasm, discharge, and selective procreation. At least that is what it is in our society.

What is the adult end point of the development of the aggressive drive? I would suggest that in our society the end point for aggressive drive development is represented ideally by the efficient functioning of those activities that provide for continuing autonomy within the context of relationships with others in the environment; expanding intellectual activity relatively free from intrusive needs; yet a freedom to satisfy these needs in creative and adaptive ways.

This end point for aggression is not universally achieved, nor is it acquired without the involvement of many other psychic functions. Indeed, if it were not for the optimum functioning of many other aspects of the psychic apparatus, we might expect to see, and do see, aggression in its less adaptive forms, ranging from the demanding, biting, torturing behavior of infants, through certain symptom formations in childhood such as soiling and bedwetting, to the outright hostile and sadistic acts that can be observed throughout childhood, adolescence and adulthood. Left unmodified, such aggression may be turned inwards or directed outward. Perhaps the most striking features of persons who engage in such acts are their immaturity and the distortion in their capacity to enjoy a satisfying love relationship—both of which arise from similar causes and similarly serve to potentiate hostile, sadistic, and masochistic acts of aggression.

Aggression and Values

We now come to the problem of values in relation to the concept of aggression just outlined, since whether we call aggression good or bad, normal or pathological, the adjective used merely connotes the value society or the individual places upon the behavior that represents the aggressive drive. There is nothing wrong with placing such a value; it is only necessary for us to be clear about the context of the value: that is, is such and such behavior good (or bad) with respect to the individual's ultimate development, the current demands of reality, the tolerance of others, etc.? For example, a child may become frustrated in his efforts to master a skill, or satisfy a need, and his aggressive drive may be mobilized resulting in further efforts. On the other hand, a massive discharge of aggression may occur in the form of an outburst of rage or temper. It is possible to see that under certain circumstances the demands of reality might leave the child no other choice (the aggression is then "good"). Or the tolerance of others may be exceeded (the aggression is then "bad"). Again, the massive discharge might represent a regression and the tendency towards poor impulse control development in the child (the aggression is then "bad"). Or the child may experience relief from an intolerable situation (the aggression is then "good").

What are the particular manifestations of aggressive drive development that lead us to label it as good or bad, especially with respect to his individual development, but also with respect to his environment?

The young infant may cry lustily, wave his arms and kick with his legs. He may also bite and later kick, hit, or torture, or nearly destroy himself, an extension of himself such as a toy teddybear, or another person. Sometimes these behavioral reactions are exacerbated when the infant is frustrated, and may be accompanied by affects of rage and hate. To the extent that these reactions are the infant's attempts at adaptation, they are "good"; to the extent that they represent a signal that the child's level of frustration has exceeded his tolerance limit, they are less adaptive. Whether or not they are considered "bad" will depend upon other factors, including the child's stage of development, the satisfactions the child otherwise receives, the duration and extent of the frustration, and the response of the environment—this latter in part determined by the tolerance of that environment. Thus, if a child is unloved, and the frustrations are prolonged and extreme, and the environment does not respond adaptively to his needs for whatever reason, clearly this aggressive behavior may be seen as a sign, or symptom, of impending deterioration—but it is not the cause of that deterioration; it is only the sign that the noxious environment is exerting a deleterious effect upon the child. On the other hand, if the aggression continues its unmodified course, then indeed it is "bad" in its own right, since the child is then vulnerable to his own aggression and may destroy himself.

As the child develops, more subtle behavioral reactions may occur in response to the need to adapt and to deal with frustration within the context of the social relationships the child must maintain. Furthermore, the child has more inner resources to call upon to withstand such noxious stimuli, and even in some cases to overcome them in advantageous ways. Adversity is often a stimulus to development just as necessity is the mother of invention. The child can be quite inventive in his discharge of aggression.

Behavioral Manifestations of Aggressive Drive

In the young infants the child may turn his aggression inwards (head banging) or outwards (temper tantrums, destructive behavior), especially when frustrated. When the child is able to manipulate his bowel and bladder functions, this too may be used in the service of discharging aggression outwardly, but in a more indirect form (soiling, wetting). Later still, especially when more subtle defenses against aggression are available to the child, more subtle manifestations of the aggressive drive may occur.

Sometimes, for example, the child will manage not to hear the request of an adult, whether parent or teacher, or his aggression may be disguised by slyness, or covered by such reaction formations as shyness and embarrassment. Occasionally a child will remove himself from any situation that invites his own aggression, or he may deny to himself as well as to others that he has ever had an aggressive wish. Occasionally the child will cunningly stick to the letter of a rule—he will do something which is allowed in one situation but which in the present situation is clearly an aggressive act. Later still, the the aggression will find expression in the form of a joke, or may actually be turned into the opposite—the child who is just too sweet and too good.

A more sophisticated use of defense mechanisms, including repression, displacement, projection, and guilt may later be used by the child to control his own aggression. For example, the child may blame others for his own aggression, or rationalize his actions. Yet at the same time, it is interesting to note that mere rational thought alone is not in itself sufficient to control aggression. Lorenz hints at the psychic structure and its source of energ that is necessary for the control of aggression in his analogy to power steering: "Like power steering in a modern car, responsible morality derives the energy which it needs to control human behavior from the same primal power which it was created to keep in rein." (Lorenz 1966a). Here superego functioning becomes an important factor in the guilt that is at times necessary in the child's developing control of his impulses, while superego functioning itself is, so to speak, motored by energy derived from the same aggressive and sexual impulses it seeks to control. Later the child may attempt to control his aggressive impulses by promising not to hit again, but his promise may outstrip his capacity to control himself. He may also subsequently experience guilt, and may even seek punishment, sometimes, by being caught for an act that represents another "crime" he believes he has committed; that is, the unconscious crime of an aggressive wish against someone he loves. Occasionally the aggression is turned inwards, culminating in self-destructive acts, including suicidal attempts, particularly during adolescence. Not uncommonly a child will use many defenses simultaneously; for example, he may project outward his aggression toward, say, a parent, displace it onto another person, the teacher, and then identify with that person as the aggressor—a kind of projective-identification. Most important, the child learns to sublimate his aggression.

Variations of Aggressive Drive Development and Behavior

Under what circumstances might an exacerbation of behavior driven by aggression occur? Or, to ask the question another way, what might lead to an intensification of frustration and aggression on the one hand, and poor impulse control on the other hand?

Five possibilities present themselves:

1. First, the aggressive drive endowment of the child must be considered. Observations in the newborn nursery reveal the enormous range of activity of infants in a standard environment. The significance of this endowment lies in the way it intermeshes with the needs and expectations of the parents once the child is in their care (Ritvo and Solnit 1958).
2. Before long, a variety of ways of stimulating the child are employed by the parents

to the good of the child's development. However, sometimes the stimulation is excessive and gives rise to frustration and aggressive tension. Such stimulation may take place in the form of spankings or provocative teasing.

3. This leads us to consider the model that the parent presents to the child. The types of model are infinitely varied, but certain broad categories can be used to define certain kinds of impacts. For example, at one extreme would be the quiet, passive parent who barely stimulates the child or who quietly meets the child's needs; at the other extreme would be the marriage characterized by violence, in which each parent himself has poor impulse control and consequently can only offer a similar model to the child.
4. Sometimes a parent will place excessive clamps on the expression of any aggressive impulse, even when it is easy to see how this suppressive attitude may exceed the child's capacity to control himself, leading to behavior which is beyond the tolerance of such parents.
5. Lastly, when there is a weak emotional tie between parent and child, there may be, so to speak, inadequate love to bind the aggression. It is as though the child has little incentive or wish to please, and acts upon his aggressive impulses with little, if any, feeling of guilt. Indeed, he may act upon them as a mode of revenge against the parent.
6. I should add a sixth possibility, and that is when the mother and father themselves have a conflict about their own aggressive impulses, and as a result are more or less paralyzed when it comes to controlling the child and setting limits. Such parents are prone to react excessively, and often inconsistently, usually on the basis of their own needs rather than those of the child.

Conclusion

In the last analysis, aggressive energy serves the child in his struggle for survival and adaptation, and the behavioral reactions observed are manifestations of the degree to which the child has been successful in this endeavor.

It becomes clear that we cannot simply label what at first appears to be a straightforward aggressive act as either "good" or "bad." Rather, it would appear to be more helpful to consider the "good" and "bad' aspects of an item of behavior with respect to the child's current developmental state, his future development, and the demands of his expanding environment. Further, any single item of human behavior is rarely purely aggressive, even in the broadest sense of the term; it is almost always fused with other sources of behavior, not the least of which are the sexual strivings of the individual. Lorenz put it well when he stated that:

> " . . . in the evolution of vertebrates, the bond of personal love and friendship was the epoch-making invention created by the great constructors when it became necessary for two or more individuals of an aggressive species to live peacefully together and to work for a common end. We know that human society is built on the foundation of this bond, but we have to recognize the fact that the bond has become too limited to encompass all that it should: it prevents aggression only between those who know each other and are friends, while obviously it is all active hostility between all men of all nations or ideologies that must be stopped" (Lorenz 1966b).

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MOTIVATIONAL AND EMOTIONAL FACTORS IN THE BEHAVIOR OF THE RETARDED[1]

Edward Zigler, Ph.D.

The behavior of the retarded is not the immutable product of low intelligence alone, and, in fact, a striking feature encountered when groups of retardates are observed is the variety of behavior patterns displayed. Clearly, we are not dealing with a homogeneous group of simple organisms. Once we concern ourselves with the total behavior of the retarded child, we find him an extremely complex psychological system. It is unfortunate that so little work emanating from a personality point of view has been done with the retarded. Some progress has been made, however, and much of the recent work supports the view that it is not necessary to employ constructs other than those used to account for the behavior of normal individuals in explaining the behavior of the familial retarded. It appears that many of the reported differences between retardates and normals of the same M.A. are a result of motivational and emotional differences which reflect differences in environmental histories, and are not a function of innate deficiencies.

That personality factors are as important in the retardate's adjustment as are intellective factors has been noted by several workers, e.g., Penrose (1963), Sarason (1953), and Tizard (1953). [See Windle (1962) for an especially comprehensive review of the importance of nonintellective factors in the prognosis of mental retardation.] Many of the earlier workers in the country, such as Fernald and Potter, felt that the difference between social adequacy and inadequacy in that large group of borderline retardates was a matter of personality rather than intelligence. A number of studies have confirmed this view. (See Windle, 1962.) Perhaps the best of these is the comprehensive study by Weaver (1946) of the adjustment of 8,000 retardates inducted into the United States Army, most of whom had I.Q.'s below 75. Of the total group, 56 per cent of the males and 62 per cent of the females made a satisfactory adjustment to military life. The median I.Q.'s of the successful and unsuccessful groups were 72 and 68, respectively. Weaver concluded that "personality factors far overshadowed the factor of intelligence in the adjustment of the retarded to military service."

The tendency to overemphasize the importance of intellect in adjustment has been made clear by Windle (1962). On the basis of a survey, he found that most institutions presume that intelligence is the critical factor in adjustment after release. Windle goes on to point out that the vast majority of studies (over 20) have reported no relation between intellectual level and adjustment after release from institutions. In examining this literature we find that the factors associated with poor social adjustment include anxiety, jealousy, overdependency, poor self-evaluation, hostility, hyperactivity, and failure to follow orders even when requests were well within the range of intellectual competence.

It is hardly surprising that retardates evidence such difficulties in light of their atypical histories. The specific atypical features of their socialization histories, and the extent to which they are atypical, may vary from child to child. Two sets of parents who are themselves familially retarded may provide quite different socialization histories for their children. At one extreme we may find a familially retarded child who is ultimately institutionalized, not because of lack of intelligence, but because his own home represents an especially poor environment. That many borderline retardates are institutionalized for just such reasons has been confirmed by Kaplun (1935) in a study of 642 high-grade retardates. Zigler's more recent finding (1961) that a positive relationship exists between the institutionalized familial retardate's I.Q. and the amount of preinstitutional deprivation he experienced provides further support for this claim.

At the other extreme, a familially retarded set of parents may provide their children with a relatively normal home even though it might differ in certain important respects—values, goals, and attitudes—from the typical home in which the families are of average or superior intelligence. In the first example, the child not only experiences a quite different socialization history while still living with his parents, but also differs from the child in the second situation to the extent that institutionalization affects his personality structure. (See Yarrow, 1964.) Given the penchant of many investigators for

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comparing institutionalized retardates with children of average intellect who live at home, the factor of institutionalization becomes an extremely important one. One cannot help wondering how many differences discovered in such comparisons reflect some cognitive aspect of mental retardation as opposed to the effects of institutionalization, the factors that led to the child's institutionalization, or some complex interaction between these factors and institutionalization.

To add even more complexity, the socialization histories of both institutionalized and noninstitutionalized familial retardates differ markedly from the history of the brain-damaged retardates. The brain-damaged do not show the same gross differences from normals in the frequency of good versus poor environments. In the face of such complexity, we need not consider the problem unassailable nor need we assert that each retarded child is so unique that it is impossible for us to isolate the ontogenesis of those factors which we feel are important in influencing the retardate's level of functioning. Once we conceptualize the retardate as occupying a position on a continuum of normalcy, we can allow our knowledge of normal development to give direction to our efforts.

This does not mean that we ignore the importance of the lowered intelligence per se, since personality traits and behavior patterns do not develop in a vacuum. However, in some instances the personality characteristics of the retarded will reflect environmental factors that have little or nothing to do with intellectual endowment. For example, many of the effects of institutionalization may be constant regardless of the person's intelligence level. In other instances we must think in terms of an interaction; that is, given his lowered intellectual ability, a person will have certain experiences and develop certain behavior patterns differing from those of a person with greater intellectual endowment. An obvious example is the greater amount of failure which the retardate typically experiences. But again what must be emphasized is that the behavior pattern developed by the retardate as a result of such a history of failure may not differ in kind or ontogenesis from that developed by an individual of normal intellect who, by some environmental circumstance, also experiences an inordinate amount of failure. By the same token, if the retardate can somehow be guaranteed a more typical history of success, we would expect his behavior to be more normal, independent of his intellectual level. Within this framework, the author will discuss the personality factors which have been known to influence the performance of the retarded.

Caution is necessary in evaluating the role of motivational and emotional factors in the performance of the retarded. Performance on a task is most appropriately conceptualized as a function of two types of factors: intellective, i.e., cognitive; and nonintellective, i.e., motivational. The contribution of each factor will vary with the nature of the task. Motivational factors will more readily influence a perserveration task, e.g., how long a retardate will continue to put marbles into a box, than they will a discrimination learning or concept-formation task, although it has been demonstrated that the performance of retardates on tasks of the latter type is also influenced by motivational factors (Butterfield and Zigler, 1965; Zigler and de Labry, 1962). Furthermore, improved performance following a manipulation of the child's motivation should not be interpreted as evidence that basic intellectual capacity has been changed. Rather, these demonstrations suggest ways in which one may help the mentally retarded to utilize their intellectual capacity optimally.

Anxiety

Considerable evidence has now been collected indicating the importance of anxiety on performance for a wide variety of tasks (Sarason *et al.*, 1960; Spence, 1958; Taylor, 1963). The attenuating effects of anxiety on performance appear to be a function of both the task-irrelevant defensive responses employed by the person to alleviate his anxiety (Mandler and Sarason, 1952; Sarason *et al.*, 1960) and the drive features of the anxiety itself. The drive approach to anxiety (Spence, 1958; Taylor, 1963), which has received considerable confirmation, conceptualizes high anxiety as beneficial on extremely nondemanding tasks, e.g., classical eyelid conditioning, but detrimental on complex tasks where a variety of responses are available to the person. The higher anxiety level of retardates, as compared with normals, has been noted by several investigators (see Berkson, 1963; Cantor, 1963; Garfield, 1963; Spradlin, 1963; Stevenson, 1963), who have either demonstrated or suggested that their heightened anxiety level could well have produced certain of the reported differences between retardates and M.A.-control normals. Work with retardates that has either focused on anxiety or raised the anxiety issue in a post hoc manner, is of considerable value "in that it applies concepts and techniques to the study of retarded individuals, which for the most part had not been applied or seen as relevant for this group" (Garfield, 1963, p. 594).

The evidence that anxiety level affects the performance of retardates as much as that of normals, and that retardates might have higher levels of anxiety than normals, tells us little about the ontogenesis of anxiety in retardates. To understand their atypical anxiety levels, we must examine the relatively atypical experiences of the retarded, as well as a variety of other motivational states which influence their performance.

Social Deprivation

It has become increasingly clear that our understanding of the performance of the institutionalized familial retardate will be enhanced if we consider the inordinate amount of preinstitutional social deprivation he has experienced (Clarke and Clarke, 1954; Kaplun, 1935; Zigler, 1961). A series of recent studies (Green and Zigler, 1962; Shepps and Zigler, 1962; Zigler, 1961, 1963a; Zigler, Hodgden, and Stevenson, 1958; Zigler and Williams, 1963) has indicated that one result of such early deprivation is a heightened motivation to interact with a supportive adult. These studies suggest that, given this heightened motivation, retardates exhibit considerable compliance with instructions when the effect of such compliance is to increase or maintain the social interaction with the adult. Compliance is apparently reduced in those instances where it leads to terminating the interaction.

Recent data suggest that the perseveration so frequently noted in the behavior of the retarded is primarily a function of this motivational factor rather than the inherent cognitive rigidity suggested by Lewin (1936) and Kounin (1941a, b). Evidence on this latter point comes from findings indicating that: (a) the degree of perseveration is directly related to the degree of preinstitutional deprivation experienced (Zigler, 1961); and (b) institutionalized children of normal intellect are just as perseverative as institutionalized retardates, while noninstitutionalized retardates are no more perseverative than noninstitutionalized children of normal intellect (Green and Zigler, 1962; Zigler, 1963a). The finding that institutionalization (or the social history factors leading to institutionalization) is the crucial factor in determining the child's response to social reinforcement on a simple task has also been reported by Stevenson and Fahel (1961). The heightened motivation to interact with an adult, stemming from a history of social deprivation, would appear to be consistent with the often-made observation of certain behaviors in the retarded; i.e., they seek attention, desire affection, etc. (Cruickshank, 1947; Doll, 1962; Hirsh, 1959; Wellman, 1938).

It is almost impossible to place too much emphasis on the role of overdependency in the institutional familial retarded and on the socialization histories that give rise to such overdependency. Given some minimal intellectual level, the shift from dependency to independence is perhaps the single most important factor necessary for the retardate to become a self-sustaining member of our society. It appears that the institutionalized retardate must satisty certain affectional needs before he can cope with problems in the manner of those whose affectional needs have been relatively satiated. Some evidence that this attenuating aspect of retarded behavior can be overcome has been presented by McKinney and Keele (1963), who found improvement in a variety of behaviors in the mentally retarded following an experience of increased mothering.

Zigler and Williams (1963) have provided some evidence that the child's motivation for social interaction and support is influenced by an interaction between preinstitutional social deprivation and institutionalization. It was found that, although institutionalization generally increased this motivation, it was increased much more for children coming from relatively nondeprived homes as compared to those coming from more socially deprived backgrounds.

An unexpected finding of the Zigler and Williams study was that a general decrease in the I.Q.'s of retardates was discovered between the administration of two I.Q. tests, the first of which occurred at the time of admission five years prior to this follow-up study. This change in I.Q. is reminiscent of a finding by Clarke and Clarke (1954). These investigators found that changes in the I.Q.'s of retardates following institutionalization were related to their preinstitutional histories. They discovered that children coming from extremely poor homes showed an increase in I.Q. which was not observed in children coming from relatively good homes. Zigler and Williams did not find I.Q. change significantly related to preinstitutional deprivation, but, consistent with Clarke and Clarke, they found that the only subjects who evidenced an increase in I.Q. were in the highly deprived group. The failure of Zigler and Williams to replicate the findings of Clarke and Clarke may be due to two factors: the subjects used by Clarke and Clarke were older and had been institutionalized at a later age; and, the I.Q. changes reported by Clarke and Clarke took place during two years of institutionalization, while the I.Q. changes reported in the Zigler and Williams study were based on five years of institutionalization. This latter factor becomes increasingly important in view of the Jones and Carr-Saunders finding (1927) that normal institutionalized children show an increase in I.Q. early in institutionalization and then a decrease in I.Q. with longer institutionalization.

The work of Clarke and Clarke, Jones and Carr-Saunders, and others (e.g., Guertin, 1949), dealing with changes in I.Q. following institutionalization, has given central importance to the degree of *intellectual stimulation* provided by the institution in contrast to that provided by the original home. The Zigler and Williams study, however, suggests that the change in I.Q. reflects a change in the child's *motivation*, and, in fact, they found a relationship between I.Q. decrement and the child's motivation for social interaction.

Positive- and Negative-Reaction Tendencies

Although there is considerable observational and experimental evidence that social deprivation results in a heightened motivation to interact with a supportive adult, it appears to have other effects as well. The nature of these effects is suggested in those observations of the retarded that have noted their fearfulness, wariness or avoidance of strangers, or their suspicion and mistrust (Hirsh, 1959; Wellman, 1938; Woodward, 1960). The experimental work done by Zigler and his associates on the behavior of the institutionalized retarded has indicated that social deprivation results both in a heightened motivation to interact with supportive adults (positive-reaction tendency) and in a reluctance and wariness to do so (negative-reaction tendency).

The construct of a negative-reaction tendency has been employed to explain certain differences between retardates and normals reported by Kounin, differences that have heretofore been attributed to the greater cognitive rigidity of retarded individuals. As one measure of rigidity, Kounin employed a task in which the subject is instructed to perform a response which he may continue until he wishes to stop; he is then instructed to perform a highly similar response until again satiated. A recurring finding in studies employing such a two-part task (Kounin, 1941a; Zigler, 1958; Zigler *et al.*, 1958) has been that retardates have a much greater tendency than normals to spend more time on task two than on task one. Zigler (1958) suggested that this was due to the greater negative-reaction tendency of retarded subjects which was an outgrowth of the more negative encounters that institutionalized retardates experienced at the hands of adults. His reasoning was that the high negative-reaction tendency of retardates was reduced as a result of the pleasant experiences encountered on task one which, in turn, resulted in a longer playing time on task two. Normals tend not to show such a pattern since there is relatively little negative-reaction tendency that can be reduced during task one.

This view was tested in a study (Shallenberger and Zigler, 1961) in which normal and retarded subjects, matched on M.A., were compared on a two-part experimental task similar to those used in the earlier studies. In addition to the basic procedure employed in these studies, three experimental games, given under two conditions of reinforcement, preceded the two-part criterion task. In a positive reinforcement condition all of the subject's responses met with success, and he was further rewarded with verbal and nonverbal support from the experimenter. It was assumed that this reinforcement condition reduced the subject's negative-reaction tendency. In a negative reinforcement condition, all of the subject's responses met with failure, and the experimenter further punished the subject by commenting on his lack of success. It was assumed that this condition increased the negative-reaction tendency. Half of the normals and half of the retardates were given the games in the positive experimental condition, while the other half of each group received the negative condition. All subjects were given the identical two-part criterion task in which they were consistently praised for all responses.

The most striking finding of this study was that, as predicted, both negatively reinforced groups spent more time on Part II than on Part I of the criterion task, while the two groups receiving the positive condition played Part I longer than Part II. The findings of this study offer further validation for the general motivational hypothesis, while also indicating a need for its extension. Future research should be concerned with the isolation of those specific events which give rise to each of these opposing motivational factors, i.e., the desire to interact and the wariness to do so.

Further investigation of such positive- and negative-reaction tendencies, their interactions, and the specific events which give rise to them may clarify issues much more global in nature than the troublesome finding that under certain conditions retarded individuals will play a second part of a two-part cosatiation task longer than the first part. Specifically the author has in mind the current controversy over whether social deprivation leads to an increase in the desire for interaction or to apathy and withdrawal (Cox, 1953; Freud and Burlingham, 1944; Goldfarb, 1953; Irvine, 1952; Spitz and Wolf, 1946; Wittenborn and Myers, 1957).

This issue has been followed up in a series of studies with children of normal intellect (Berkowitz, Butterfield, and Zigler, 1965; Berkowitz and Zigler, 1965; McCoy and Zigler, 1965) directed at further validation of the "valence position." Stated simply, this position asserts that the effectiveness of an adult as a reinforcing agent depends upon the valence he has for the particular child whom he is reinforcing. This valence is determined by the child's history of positive and negative experiences with adults. The studies noted above have produced considerable evidence that prior positive contacts between the child and the adult increase the adult's effectiveness as a reinforcer, while negative contacts decrease it. If the experimentally manipulated negative encounters in these experiments are conceptualized as the experimental analogue of what institutionalized retardates actually have experienced, then the often-reported reluctance and wariness with which such children interact with adults becomes understandable. A logical conclusion here is that wariness of adults, and of the tasks that adults present, leads to a general attenuation in the retarded child's social effectiveness. Failure of institutionalized retardates on tasks presented by adults is therefore not to be attributed entirely to intellectual factors. The high negative-reaction tendency motivates him toward behaviors, e.g., withdrawal, that reduce the quality of his performance to a level lower than that which one would expect on the basis of his intellectual capacity alone.

Failure and the Performance of the Retarded

Another factor frequently mentioned as a determinant in the performance of the retarded is their high expectancy of failure (Cromwell, 1963). This failure expectancy has been viewed as an outgrowth of a lifetime characterized by frequent confrontations with tasks for which the retarded are intellectually ill-equipped to deal. That failure experiences and the failure expectancies to which they give rise affect a wide variety of behaviors in the intellectually normal has now been amply documented (Atkinson, 1958a, b; Katz, 1964; Rotter, 1954; Sarason *et al.*, 1960). Of special interest to workers in the area of mental retardation is Lantz's (1945) finding that a relatively simple failure experience prevented children from profiting by practice which ordinarily leads to improvement on intelligence test scores.

The results of experimental work employing the success-failure dimensions with retardates are still somewhat inconsistent. The work of Cromwell and his colleagues (Cromwell, 1963) has lent support to the general proposition that retardates have a higher expectancy of failure than do normals. This results in a style of problem-solving for the retardate which causes him to be much more motivated to avoid failure than to achieve success. However, the inconsistent research findings suggest that this fairly simple proposition is in need of further refinement. One investigator (Gardner, 1957) found that retardates performed better following success and poorer following failure as compared to a control group. Another investigator (Heber, 1957) found that the performance of normals and retardates was enhanced following both a failure and a success condition, although in the success condition the performance of retardates was enhanced more than that of normals.

Conversely, Kass and Stevenson (1961) found that success enhanced the performance of normals more than that of retardates. Another study also found that failure had a general enhancing effect for both normals and retardates, but that failure enhanced the performance of normals more than that of retardates (Gardner, 1958). In a recent study by Butterfield and Zigler (1965), one factor which may have produced this type of inconsistency was isolated. These investigators found that both normal and retarded children reacted differentially to success and failure experiences as a function of their responsivity to adults, i.e., their desire to gain an adult's support and approval. The nature of the difference between normals and retardates in their reaction to success or failure experiences appeared to be determined by this latter variable. Among high responsive subjects, failure, as compared with success, attenuated the performance of the retarded while improving the performance of normal subjects. Among low responsive subjects, failure, as compared with success, attenuated the performance of normals while improving the performance of retardates.

The debilitating effects of prolonged failure on the performance of the retarded have been found by Zeaman and House (1960). These investigators discovered that following such failure retardates were unable to solve a simple problem although they had previously been able to do so. Assuming a failure set in retardates, Stevenson and Zigler (1958) confirmed the prediction that retardates would be willing to "settle for" a lower degree of success than would normal children of the same mental age. The fear of failure in the mentally retarded also appears to be an important factor in differences that have been found between normals' and retardates' achievement motivation (Jordan and DeCharms, 1959).

Recent studies (Green and Zigler, 1962; Turnure and Zigler, 1964; Zigler *et al.*, 1958) have indicated that the high incidence of failure experienced by retardates generates a cognitive style of problem-solving characterized by outer-directedness. That is, the retarded child comes to distrust his own solutions to problems and therefore seeks guides to action in the immediate environment. This outer-directedness may explain the great suggestibility so frequently attributed to the retarded child. Evidence has now been presented indicating that, compared with normals of the same M.A., the retarded child is more sensitive to verbal cues emitted by an adult, is more imitative of the behaviors of both adults and peers, and engages in more visual scanning. Furthermore, certain findings (Green and Zigler, 1962) suggest that the noninstitutionalized retardate is more outer-directed in his problem-solving than the institutionalized retardate. This makes considerable sense if one remembers that the noninstitutionalized retardate does not reside in an environment adjusted to his intellectual shortcomings and should therefore experience more failure than the institutionalized retardate.

Turnure and Zigler (1964) have suggested that the distractibility so frequently encountered in the retarded reflects, in part, this outer-directed style of problem-solving. This interpretation is of particular interest, since distractibility has often been viewed as a neurophysiologically determined characteristic of the retarded rather than the reflection of a style of problem-solving emanating from the particular experiential histories of such children. Work on the outer-directedness of the retarded also appears related to the locus of control work done by Cromwell and his associates (reviewed in Cromwell, 1963). These investigators found that retardates, as compared with normals, manifest an external locus of control, i.e., they attribute certain events, caused by their own behavior, to outside forces over which they have little control. (This internal-versus external-control dimension has been employed by Cromwell to bring some further order to the inconsistent findings in the success-failure literature.)

The Reinforcer Hierarchy

Another nonintellective factor important in understanding the behavior of the retarded is the retardate's motivation for various types of incentives. That performance by normals and retardates on a variety of tasks is influenced by the nature of the incentive is certainly well documented (Cantor, 1963). The social deprivation work discussed earlier in this section indicates that retardates have an extremely high motivation for attention, praise, and encouragement. Several investigators (Beller, 1955; Cromwell, 1963; Gewirtz, 1954; Heathers, 1955; Zigler, 1963b) have suggested that, in normal development, the effectiveness of attention and praise as reinforcers diminishes with maturity, and is replaced by the reinforcement inherent in the information that one is correct. This latter type of reinforcer appears to serve primarily as a cue for the administration of self-reinforcement.

Zigler and his associates (Zigler, 1962; Zigler and de Labry, 1962; Zigler and Unell, 1962) have argued that a variety of experiential factors in the history of the retarded cause them to be less motivated to be correct, simply for the sake of correctness, than normals of the same M.A. Stated somewhat differently, these investigators have argued that the position of various reinforcers in the reinforcer hierarchies of normal and retarded children of the same M.A. differ. To date, the experimental work of this group has centered around the reinforcement which inheres in being correct. It is this reinforcer that is the most frequently dispensed, immediate incentive in most real-life tasks. Furthermore, it is a frequently used incentive in many experimental cognitive and perceptual tasks on which retardates and normals are compared, and it also seems to be the most important incentive in the typical test situation. When such an incentive is employed in experimental studies, one wonders how many of the differences found are attributable to differences in capacity between retardates and normals, rather than to differences in performance which result from the different values that such incentives might have for the two types of subjects.

Clearest support for the view that the retardate is much less motivated to be correct than is the middle-class child, so typically used in comparisons with the retarded, is contained in a study by Zigler and de Labry (1962). These investigators tested middle-class, lower-class, and retarded children *equated on M.A.* on a concept-switching task (Kounin, 1941a) under two conditions of reinforcement. In the first condition, similar to that employed by Kounin, the only reinforcement dispensed was the information that the child was correct. In the second condition, the child was rewarded with a toy of his choice if he switched from one concept to another. In the "correct" condition these investigators found, as Kounin did, that retardates were poorer in the concept switching than were middle-class children. That this was not a simple matter of cognitive rigidity was indicated by the finding that lower-class children equated on M.A. with the middle-class children were also inferior to the middle-class children. In the toy condition this inferiority disappeared, and retarded and lower-class children performed as well as the middle-class children. This study highlights an assumption that has been noted as erroneous by many educators; namely, that the lower-class child and the retarded child are motivated by the same incentives that motivate the typical middle-class child. An intriguing avenue of further research is the degree to which the position of various reinforcers in the hierarchy can be changed.

General Effects of Institutionalization

No discussion of motivational factors in the performance of the retarded would be complete without some mention of the effects of institutionalization. The institutionalization variable has probably contaminated more research in the area of mental retardation than any other single variable. Given our general lack of knowledge concerning the effects of institutionalization on human behavior, the extent of this contamination cannot be determined. That the effects of institutionalization on the behavior of retardates are considerable has been suggested by several investigators (Guskin, 1963; Lipman, 1963; McCandless, 1964; Nye, 1958; Sarason and Gladwin, 1958; Spradlin, 1963; Windle, 1962). In view of the general consensus concerning its importance, it is amazing that more work has not been done to investigate the effects of institutionalization on retarded children.

Some fairly clear findings with retardates have demonstrated that institutionalization causes a decrement in the quality of language behavior (Lyle, 1959; Schlanger, 1954), reduces the level of abstraction on vocabulary tests (Badt, 1958), interferes with the ability to conceptualize an emotional continuum (Iscoe and McCann, 1965), and increases the child's orientation toward punishment (Abel, 1941). These studies, though suggestive, have shed little light on the specific aspects of institutionalization which affect such behaviors or on the exact nature of the process through which behaviors are affected. Whether the deficiencies in the behavior of the institutionalized retardate are motivational in nature or reflect an actual change in intellectual capacity is still an open question.

Evidence that institutions for the retarded differ in their effects on behavior has recently been reported by Butterfield and Zigler (1965). It was found that children residing in a cold, restrictive institution showed a higher motivation for adult support and approval than children residing in an institution having a warm, accepting social climate. These investigators are presently conducting a cross-institutional longitudinal study of six state schools for the retarded in an effort to isolate the institutional factors and psychological processes underlying such effects.

Much of this work on motivational and emotional factors in the performance of the retarded is very recent. The research conducted on several of the factors discussed in this section is more suggestive than definitive. It is clear, however, that these factors are extremely important in determining the retardate's level of functioning. Furthermore, these factors seem much more open to environmental manipulation than do the cognitive processes discussed earlier. An increase in knowledge concerning motivational and emotional factors and their ontogenesis holds considerable promise for alleviating much of the social ineffectiveness displayed by that rather sizable group of persons who must function at a relatively low intellectual level.

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Footnote

1. Preparation of this article was facilitated by Research Grant MH-06809 from the National Institutes of Mental Health, United States Public Health Service, and by the Gunnar Dybwad Award of the National Association for Retarded Children.

MINIMAL BRAIN DAMAGE AND PERSONALITY DEVELOPMENT IN CHILDREN

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Within the past decade, professional interest has focussed on the role of the syndrome of "minimal brain damage" in the genesis of children's learning disabilities. The syndrome, its etiology, diagnosis, the intellectual deficits and behavioral deviations which accompany it, have been discussed in detail in a recent article by Pincus and Glaser[1] which includes a comprehensive bibliography, and by Graffagnino[2] in this journal. Since these reviews, as well as the main body of literature on the subject, have dealt primarily with the impact of such organicity on the learning process and on behavior, it will be the purpose of the present article to focus on the impact of minimal brain damage on the child's personality development.

A central problem in the development of the child with minimal brain damage is that, unlike severe brain damage which may result from birth injury, head trauma, or disease, and which is readily observable and easily diagnosed, minimal organicity may not be so readily recognized. Pincus and Glaser[1] state that "The term 'brain-damaged child' or, more quantitatively, 'minimally brain damaged,' as used currently is, in fact, merely a label for certain kinds of aberrant behavior. . . . The phrase implies structural or organic changes with physiologic dysfunction; yet the diagnosis is used to describe behavior that may have no consistent anatomic, electrophysiologic, biochemical, or neurologic correlates."

A recent publication of the U. S. Department of Health, Education and Welfare[3] lists approximately one hundred symptoms which may characterize the child with minimal brain dysfunction. Of these, the ten symptoms most frequently cited in order of importance are: hyperactivity, perceptual-motor impairments, emotional lability, general coordination deficits, disorders of attention, impulsivity, disorders of memory and thinking, specific learning disabilities, disorders of speech and hearing, and equivocal neurological signs and electroencephalographic irregularities.

Further, numerous authors have pointed out that not only are the behavioral characteristics of the minimally brain damaged child many and varied, but also that the timing of the injury with respect to the stage of development of the child may well be crucial in his subsequent development.

As Lewis[4] has noted, "The syndrome of brain-damage can now usefully be regarded as a result of a dynamic interaction involving numerous factors, such as the degree and timing of the original brain-injury; the psychological state of the child and his parents before, during and after the injury; the meaning of the injury to both child and parents; the prevailing conditions which may aggravate or relieve the symptomatic behavior; and the attitudes adopted by both child and parents in attempting to deal with the situation."

Of these factors, the present paper will focus on "the attitudes adopted by both child and parents in attempting to deal with the situation" and the influence of these attitudes on the child's developing personality from infancy through adolescence.

Infancy

In the infancy period, the deleterious effects of minimal brain damage may first be manifested in the developing mother-child relationship.

The manner in which minimal organicity may influence the interaction between mother and child has been well described by Prechtl:[5] "There is no doubt that a baby with severe brain damage may cause psychological difficulties in a mother. However, there is a broad range of minor abnormalities of the central nervous system . . . which, although they change most of the infant's behavior patterns distinctly, are not alarming enough for the mother to consult a physician right away. Nevertheless, such a child can irritate his mother considerably and give her an overanxious, overprotective or rejecting attitude towards her child. The hypokinetic child, who is very often hypotonic, drowsy, and apathetic, sucks slowly and poorly and responds only very weakly to various stimulations. Since the baby is hypotonic, the mother is sometimes fright-

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ened that she may harm the floppy baby in the bath or while swaddling him. Quite another picture is given by . . . the 'hyperexcitability syndrome.' The babies belonging to this category are hyperkinetic, often hypertonic, cry more than normal babies, show sudden changes of state from being drowsy and difficult to arouse, to being wide awake, crying and difficult to pacify. . . . Because of the low threshold of the Moro response these babies react to the approach of every person with a Moro response. This often gives mothers the impression of having frightened their baby."

In a longitudinal study of a group of hyperexcitable children and a matched control group, Prechtl[5] found that the symptoms of hyperexcitability persisted for several months after birth and that the mothers of the children in the pathological group developed a more protective and dominant relationship to their children than did the mothers in the control group. Further, in the neonatally abnormal group forty percent of the mothers expressed concern and worry about their children, while in the neonatally normal group only ten percent of the mothers did so. One can speculate that the more protective relationship developed by the mothers of the hyperexcitable children may have constituted a reaction formation to deal with the heightened ambivalence engendered by such an infant. In any event, as Prechtl concludes, "Neurologically abnormal babies do not make adequate partners in the child-mother interaction."

Minimal brain damage has also been implicated as a causal factor in the more serious psychological disturbances of infancy and early childhood, psychosis and autism. Eaton and Menolascino[6] make the point that "In chronic brain syndrome with psychosis, etiologies range from . . . minimal cerebral dysfunction to massive damage involving multiple areas." Recently, several papers have suggested that hyperoxia with resulting damage to the reticular formation may produce the syndrome of infantile autism.[7,8] However, the relative contribution and interaction of early sensory deprivation, parental understimulation, and a genetically determined susceptibility to an organic lesion have not as yet been clarified.[9] As Provence points out in her paper, "The use of developmental tests in the diagnosis of autistic disorders,"[10] it is particularly difficult to make a differential diagnosis between such causal factors as severe sensory defects, severe affect deprivation, organic brain damage, and congenital cerebral defect with mental deficiency and autistic symptoms. However, she estimates that approximately one-third of the atypical children seen by her manifest some type of organic disorder.

In the brain damaged infant, it appears probable that one basic cause of psychological problems is his inability to screen out stimuli. Gross overstimulation can, in many ways, be as damaging to a developing organism as can sensory deprivation. By not being able to screen out unimportant or extraneous stimuli, the infant is inundated by perceptual possibilities. In an effort to solve his dilemma and evade the impinging stimuli, the infant may become hyperactive in an almost literal attempt to "run away," or may withdraw into himself in an effort to pretend that the stimuli do not exist. Goldfarb,[11] Bergman and Escalona,[12] Taft and Goldfarb,[13] as well as others have described children who withdrew and seemingly became psychotic because of the effect of early brain damage or excessive sensitivity to early environmental stimulation.

While such an extreme reaction as autism is relatively uncommon in infancy, nevertheless the adjustment problems which face the minimally damaged infant and his frustrated and confused parents may lead to the development in the child of a debased self-image even before he feels the impact of formal schooling which will make more explicit deficits in his intellectual and behavioral functions.

Pre-School

In the pre-school years, many aspects of the damaged child's behavior may combine to make him feel different from his peers and to incur the disapproval and disappointment of parent and authority figures. Among these may be that his development is slower than that of his age mates; that his increased activity and distractibility may disrupt peer relationships; and that his hyperactivity, poor motor coordination, and emotional lability may lead to "difficult" and unintentionally destructive behavior. As a result of their often unfortunate explorations of the world about them, some such children may withdraw from new challenges, and become social isolates or play with younger children. Others, however, may continue their activity and when they do not respond to the efforts of parents to set limits on their behavior, may be regarded as deliberately mischievous.

Thus, Graham, Ernhart, Thurston, and Craft[14] found differences between children judged anoxic at birth and presumably minimally brain damaged, and matched controls to exist at three years of age both in cognitive functions and in behavior traits.

When parents and psychological examiners were asked to rate the children on a series of traits assumed to be associated with brain injury (activity, impulsivity, demandingness, distractibility) and with maladjustment (infantilism, negativism, fearfulness), "on the whole the anoxic group was rated less favorably than the normal group by both parents and examiners." In another study using a heterogeneous group of brain damaged but not generally retarded children,[15] it was found that the hyperkinetic personality syndrome which has been described as characteristic of the brain injured child[16] was more common among brain damaged than among normal children, but also that unfavorable personality chracteristics of a hypokinetic nature such as inactivity, infantilism, compulsiveness, and inwardness were equally common.

School Age

By the time the child reaches school age, therefore, he may already have begun to develop a self image which has many negative characteristics. Now, within the school situation, minimal organicity may manifest itself not only in intellectual deficits which disrupt school achievement, but also in deficits in fine and gross motor functions which will handicap him in his relationship to other children. Not only his learning difficulties but rejection by the group when engaging in play and sports activities may lead him to think of himself as different from his peers, and to develop the self concept that he is impaired. Clinical experience suggests that with boys in particular, the awkwardness and clumsiness which often accompany minimal brain damage may intensify feelings of inferiority because of the premium placed by the American culture on a boy's success in athletic activity. It is possible that it is the combination of such a cultural demand together with their greater susceptibility to minimal brain damage in the neonatal period[5] which accounts in part for the higher proportion of boys than girls referred to child guidance clinics.

Further, another dilemma for the minimally brain damaged child is that in many areas he retains his original intellectual potential and skills, and consequently is more painfully aware of his deficits than would be a more massively damaged or retarded child. The degree of frustration he experiences when he recognizes that he cannot express his ideas with any degree of verbal fluency or execute motorically his grasp of performance tasks, is an additional factor in the development of a sense of inadequacy and inferiority. As Zigler[17] has suggested for the retardate, in addition to the primary physical manifestations of minimal brain damage which disrupt his behavior, the secondary failure experiences which the child meets in various life situations and his constant confrontation of his deficits are an additional and serious deterrent to the development of an adequate self image.

This probability is suggested by a further study of the group of anoxic children described above. When they were evaluated at age seven,[18] significant differences in intellectual function were found between the anoxic group and the normal group in vocabulary skill, reading ability, and perceptual-motor functions. Of equal importance for personality development, however, was that the anoxic children were rated as more maladjusted by their parents, and as poorer in motor coordination by their teachers. Further, the anoxic group showed a significant impairment in social competence as this is measured by the Vineland Social Maturity Scale, as they obtained significantly lower scores in the areas of Self Help, Occupation, and Socialization. In general, therefore, the anoxic children showed more dependent behavior than did the normals, possibly because of anticipation of failure if they showed more initiative.

Finally, in estimating the extent to which minimal organicity contributes to and culminates in emotional disturbance in school age children, clinical experience indicates that a high proportion of children seen in child guidance clinics show patterns on psychological tests which are consistent with minimal central nervous system defect or injury. In fact, the statement has been made that for one clinic within the New Haven area, about twenty-five percent of the children referred as "emotionally disturbed" are found to have neurological impairment as a significant etiological factor.[19] In another survey of emotionally disturbed children seen in a child guidance clinic in Detroit,[20] approximately seventy-eight percent of the children demonstrated undeveloped or inadequately functioning perceptual-motor skills. In still another survey of 150 children attending a child guidance clinic,[21] fifty-nine percent were diagnosed as brain damaged. It would appear that the incidence of brain damage among children with behavior problems is much higher than has been suspected in the past.

Adolescence

In a paper presented at the 1967 meeting of the American Orthopsychiatric Association, Pollack[22] aptly summarized the current status of research on the role of minimal brain damage in emotional disturbance in adolescence: "Recently, several investigators have demonstrated that neurological signs indicative of central nervous system damage are significantly higher in hospitalized adolescent psychiatric patients than in normals. Hertzig and Birch[23] found neurologic dysfunction four to eight times more frequently on clinical examination in the psychiatric patients. Larsen[24] states 'The significantly higher incidence of physical and neurological deficits among . . . adolescent patients suggests that hospital psychiatric diagnoses may incompletely reflect the comprehensive diagnostic picture.' " Supporting this formulation are the results of a study by Pollack, Levenstein, and Klein[25] which showed that in a population of hospitalized schizophrenic patients, twenty-six percent were diagnosed as having suggestive evidence of central nervous system abnormality.

Pollack postulates that the early behavioral patterns of socially inappropriate and infantile behavior which characterize the brain damaged child are in adolescence exacerbated by the sexual, social, educational, and occupational challenges of impending adulthood. The consequence is a breakdown of adaptive mechanisms and the onset of severe psychopathology.

Treatment

Since there is as yet no evidence that the underlying neurological deficit can be corrected in the minimally brain damaged child, resolution of some of his frustrations and those of his parents will have to depend on other therapeutic techniques. As several authors have pointed out,[1,2,19] the first of these is to give adequate explanation to the parents and others concerned with the child, particularly his teachers, of the basis for his learning and adjustment difficulties. As has been stated by Gurwitt,[19] "Parents of such children are often confused, angry, discouraged, and depressed. Such parents often feel guilty, having conceived of themselves as totally responsible for their child's difficulty. When the various etiological factors are teased apart and the parents can see how a specific pattern has resulted they often are able to take on a more constructive parenting role."

First, therefore, the parents must be helped to understand the extent of their child's problem, and what he can be expected to accomplish. Second, the need for consistency and realistic goals should be emphasized. Both the parents and the school must be helped to understand the importance of limitations of distractions, reduction of stimuli, involvement of multiple sense modalities in learning, the introduction of small, sequential increases of abstraction, and relatively brief periods of instruction.

Most minimally brain damaged children do not need referral to a child psychiatry clinic. When they do, neurological and psychological evaluations are important in order to evaluate the extent of the defect prior to treatment. In children with deficits in attention, memory, and language, the traditional psychotherapeutic approach must be modified.[26] Rather than conversation or unstructured play, the actual therapy often utilizes form boards, balancing toys, hand-eye coordinate games, and musical instruments. Frequent consultations with the school, the use of community agencies to ease the child into new activities, and the appropriate use of tutors are important adjuncts to the direct work with the patient.

Summary

When minimal brain damage is diagnosed or suspected in childhood, as much concern should be directed to its impact on the developing personality as to its effects on learning and behavior. For though the role of such damage may be recognized in learning deficits, its contribution to a debased self image because of frustration and failure experience in other life situations may be overlooked. Following upon diagnosis, careful evaluation should be made of the child's life situation, with a view to minimizing those circumstances in which his deficits are most handicapping and maximizing those in which he can have a success experience which will bolster his ego. The parents, physician, and school share the task of continuing positively to structure the child's environment in order to enhance his growth and maturation through an optimal level of stimulation.

Finally, if secondary emotional problems are deep seated and persistent, individual psychotherapy may be indicated, using techniques adapted to the needs of the brain damaged child.

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THE IMPACT OF BLINDNESS ON THE DEVELOPMENT OF THE CHILD

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Within the past decade there have been several important advances in the study of the effects of blindness at birth or in the early weeks of life on the development of the child. Fraiberg, et al[1,2] in Ann Arbor, Burlingham[3,4] and Sandler[5] in London, and Omwake and Solnit[6] in New Haven are among those who have contributed studies examining case material with a view to learning more about the impact of this condition on the development of the ego functions in children thus handicapped. These particular researchers have been concerned with the observation of very young blind children whose progress could be followed through a longitudinal approach. Earlier there had been important contributions from the fields of social welfare, education and special education which had psychological import but which dealt largely with the problems of adjustment of older blind children or of blind adults. These earlier writers were also more concerned with the work being done with and for the blind than with the psychodynamics of the condition. The recent emphasis in the study of human growth and development on the very early relationships as playing a role of paramount significance in ego development has inspired a closer look at the effects of a recognized sensory defect on the formation of early relationships. The fact that parents, physicians, educators and social workers are now actively seeking useful knowledge and ideas for environmental support of blind babies and their families as well as for older individuals with this handicap offers a clear indication for continued intensive study of the *first* signs of possible effects of blindness on the development of the individual and on his environment. Investigation of the more readily observed aspects to early development such as motor skills, adaptive behavior and language must be implemented with study of the individual's relationships, ideas, knowledge and other cognitive skills as these emerge during the growth process. The current emphasis on the preventive aspects to all mental health problems is another indication of the need for early investigation into the psychological factors in the experiences of blind infants.

The matter of the reversibility of the various ego problems concomitant to blindness will continue to be an important subject for inquiry. Theorizing in regard to the dynamics of blindness has resulted in differences of opinion although there is unquestioned agreement as to the enormity of the problem the condition presents to the individual who is blind and to his environment. Some writers suggests that the sensory restriction causes an ego defect.[1,3,5,6] Others believe that it is rather the isolation from the environment caused by the lack of visual contact with it that creates the problem. Klein[7] for example makes the distinction as follows: "interpersonal isolation *without* sensory interference can produce symptoms; sensory deficit alone, without affective and interpersonal isolation, need not."(p. 83) With continued study more new theories are likely to be posed, although the low incidence of blindness under conditions in which it can be closely and continuously examined contributes to a problem in data collection. Fraiberg's recent and thorough studies of the role of sound in the search behavior of infants is highly significant in our present knowledge and promises interesting material on the influence of blindness on concept formation as well as on the sensori-motor experiences.[2]

Inspired by Sandler's comments on the irreversibility of egocentricity in blind persons[5] this paper will deal mainly with an especially intriguing aspect to the study of the effects of blindness on ego development—the role of vision in the first experience in relating to another person, namely, the mother. According to Dr. Sandler, ". . . it is highly probable that the basic pull toward self-centeredness and the modes of gratification characteristic of the first phase of life will always be present."(p. 359) Because the high degree of egocentricity ordinarily observed in blind persons of any age is regularly of concern to their families, teachers and friends, it should be worthwhile to explore its history and indicate some of the forms it may take in the various phases of development. Material from studies of a blind boy (Marc) and girl (Anne) who were well known to the writer throughout their childhood years will be used for illustrative purposes. The boy retained a very slight light perception but

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by the age of three months it was obvious to those who cared for her that the girl had none.

A first consideration in regard to the subject of early effects is that of the several types of deprivation to which the blind newborn is exposed. Even within the first weeks of life a sensory defect and the reduction of sensory stimulation contribute to deprivation of experiences central to the support of continuing development of the ego functions. In addition to the developmental failure of the visual system and the lack of stimulation from the environment, it might be speculated that the blind infant is even more vulnerable than the normally equipped child to the effects of *maternal* deprivation. The degree of this type of deprivation would vary according to the mother's ability to provide the psychological support required in the need for empathy, additional attention and emotional acceptance into the family group of a child with a handicap so pervasive as blindness. There exists the possibility that knowledge of the baby's blindness may affect the mother in such a way that her own ego functioning is reduced. As the significance of the defect becomes increasingly meaningful in the early months of the infant's life her depression already experienced by the infant may become apparent to others and to herself. At a time when imagination, problem solving and adaptive powers are most needed by her in order to supply experiences which involve the baby with his external environment, her energies may be fully engaged in dealing with her feelings of sadness, anger, and fear for her own and her child's future. Perhaps this is a time when a person outside the family or another family member could be especially helpful in stimulating the baby to handle toys, listen to sounds, move into new positions, and reach out to explore his boundaries. The mother's teaching function is the most likely to be impaired if she is depressed, so if ever a young baby needs a special teacher it would be under these conditions. If ever a mother needs additional psychological support to face her ambivalence and learn to deal with her unacceptable and confused feelings, it would be under these conditions. Further, because the mother is, in a sense, "in charge of" the total environment, she could well be in need of a type of guidance which would enable her to help other family members in regard to their problems of relating to a blind brother or sister. The family physician, if aware of the problems, might be in the best position to lend the needed support through the follow-up care of the new infant and other family members.

With this in mind it would seem that, although its full impact on the child's surroundings is not felt until sometime later, as a problem in development blindness becomes active from the beginning. It has been usual to delay planning for remedial measures until such time as vision is considered to be useful and necessary to the individual. The peripheral vision of the neonate, permitting awareness of brightness and dimness and the vague outline of objects, is not ordinarily viewed as essential to the young infant's comfort or progress in physical ways. Active concern develops in later weeks when clues to the child's developmental status include binocular vision and the ability to focus sharply on both stationary and moving objects. Concern for the baby's future adjustment and performance burgeons when the ability to interpret visual representations, an important aspect to cognition, is absent.

In the period when peripheral vision is the only function of the visual system, it should be recognized that even this limited opportunity to use the eyes serves to bring the infant into contact with his surroundings. Sometimes the baby seems to be holding his eyes open briefly as if to sustain the experience. In any event, no one needs to open his eyes to the world because he can do it for himself—that is, if he is not blind. Thus, the experience in forming relationships with something outside oneself has begun. Further, the nature and quality of such relationships and the differences in the life experience for those who are blind and those who are not already begin to take shape.

Whatever remedial measures the environment can produce which are appropriate in developmental terms should be made available as soon as the baby's wakeful moments can be recognized. Whatever auditory and tactile-kinesthetic approaches serve to elicit a response should be studied for their usefulness in establishing relationships both with people and with things. Whipple[8] refers to the infant's cry as an important maternal activator. It might be speculated that the newborn's eye movements, however wandering as they feebly follow light or the human face, also serve as maternal activators because they involve the attention and invite the response of the person who cares for him. It is also interesting to consider a possible relationship between the developing ability to focus the eyes and the developing mouth muscle activity which results in a smile. Instinctual in the beginning the smile becomes a learned response extraordinarily useful to the individual at any age in helping himself to get what he needs from other people. Although it is entirely possible for the mother of a blind infant to know that as the months go on her baby smiles at her in response to the way she feels or sounds to him, for most mothers the feeling that he *knows* her develops from an ability to focus his gaze on her face. Bowlby[9] suggests that the social smile is activated by two bright dots in the infant's field of vision and that these 'dots' are usually the mother's eyes. Where vision is present mother and baby can be mutually successful in making each other smile in response to a visual clue. Attention to the human face as an early sign of social responsiveness is regularly reinforced by those who care for the infant through the "smiling exchange." It is probably safe to say that the baby's gaze keeps the mother smiling and responding more than the reverse. One mother reported that the sight of her baby's unresponding eyes made her feel like turning away. Mothers of blind babies can perhaps be encouraged to discover the sensations that bring the smile to the baby's face as a way of learning to know which stimuli are most likely to bring a response. These could include gentle stroking, vigorous patting, murmuring, laughing, singing loudly, singing softly, etc.

A six-year-old blind girl who had great empathy for anything helpless loved to play 'mother' to her doll. On one occasion she worked very hard at perfecting the sound of an infant "gurgling." She said that it had to be "just right" because that was how a mother would know if her baby was "pleased." She also insisted upon careful demonstrations and adjustments of a baby being held on the shoulder because it was essential that her effort be "just like a mother would do it." Her insistence on preciseness in these simple matters illustrates the need for strong tactile-kinesthetic as well as auditory clues in mother-child communication in cases where the visual clues are lacking.

Another circumstance of infancy lending support to the idea that vision is important in the early establishment of interpersonal relationships the tendency for adults to want to see the newborn when he is awake (with his eyes open) in order to acquire a full "sense" of him. Mothers say: "Wait until he wakes up; that's when he's cute." They often coax the sleepy, yawning infant to open his eyes to show him off fully. Recently a newborn's mother was heard to say to her baby in the midst of a yawn: "Your gums aren't very pretty; show grandma your eyes." This too suggests that the child is considered to present himself to best advantage when open eyes are part of the picture of the face. An early report of infant progress is often: "He's beginning to look around." and "I think he sees me." "Of course, his eyes are shut most of the time" is sometimes offered in tones which sound apologetic—as if the baby were remiss in behavior or deficient in some way.

It is interesting to note, in this connection, that later in life adults who are trying to hold the attention of children while they are teaching, scolding, or otherwise pressing a point, frequently insist: "Look at me!" implying that they can't be certain that they are being heard if the direct glance doesn't convey attentiveness. One teacher was recently heard to say: "How can I talk to you when you aren't watching me?" "Look me in the eye and say that" is another expression which suggests the importance of the visual response in interpersonal matters. Anne once said: "Show me how to look while I'm listening" when she was trying out not being blind in order to understand her "difference" as she was becoming aware that it did exist.

In the history of the child's interpersonal relationships and the moving away from complete self-centeredness, the giving as well as the taking aspect is as important in the first instances as it becomes later on when there are more recognizable forms of mutual exchange of awareness of each other when two people are together. In the case of the blind infant it is as if he cannot "give back" to his mother with a look as can the one with even rudimentary peripheral vision. It is indeed a difficult task for the people who care for the child to learn a new type of approach to forming a relationship with another person when that person cannot take in or give out visually. How effectual the parents and others become in learning to use their voices, their hands and all parts of the body which comprise the equipment for holding and loving a baby to convey meaning and feeling will be of great significance in the early important stages of ego formation.

Around the middle of the first year when maturation and environmental support can combine to make the baby sit up, reach out and listen for familiar sounds, the parents' ability to help will depend upon their imagination, skill, and effort in finding ways to both stimulate and gratify their child's interest in his surroundings. When signs of interests in the world within reach do appear it is a further challenge to help the child find meaning in the simple experiences which serve to introduce him to the world of things, events, and personalities. One basic limitation of the blind child is in relation to the narrow range of experiences. Even when hearing and tactile-kinesthetic equipment are unimpaired there is still much that these sensations cannot convey. Whipple suggests that a sound cannot give any conception of shape, size, and physical characteristics to the infant who does not yet know of what things are made.[6] The baby is thus restricted in his ability to move about.

This limitation in motor development is compounded by the fact that he must therefore remain dependent on others for simple maneuvers which his sighted agemates are able to manage without assistance. Sight seems to provide the incentive to reach out to the environment. The blind baby's reaching out can bring him little pleasure and has the possibility for much physical pain unless either he or the environment is fully protected with safeguards against falls, burns, bruises, etc. The ordinary environment, then, does not appear to gratify the blind child, thus encouraging him to explore it. Fraiberg observes from experience with a variety of cases:[2] ". . . that sound is not an equivalent of vision in search, in reaching, in attaining an object."(p. 356) She suggests that sight is a necessary component of the sensory apparatus in constructing an object world.

So far as the need for special environment support in the early weeks of life is concerned, the preparation of the adults for the role they must play is an important feature of the long-range planning required to meet the unique needs of a blind person. It is obvious that in the newborn period the blind infant can be kept physically comfortable through relieving inner tension with food, warmth and gentle handling, just as can the one who is not blind. During these weeks it is more likely the adults who "suffer" the loss of visual contact rather than the infant himself who merely "experiences" it in an affectless way. The simple failure of the baby to follow the light or blink when his eyes are open can, however, have a powerful psychological effect upon the environment. The danger for the baby is that there is a strong likelihood that the mother and infant will reinforce each other's withdrawal, just as, under normal conditions, they can reinforce each other's responsiveness. The drawing of the seeing baby's attention outward through encouraging him to look at his mother's face, even though in the beginning it may be for her gratification rather than his own, is the first step in the lifelong process of dealing with the powerful pull toward egocentricity. It would appear to be a more slowly developing process for the blind person to learn to give out to another person than for the normally equipped. An interesting philosophical question suggested by this line of thought is whether or not pleasure in giving or exchange is an essential component of a mutually meaningful relationship.

Perhaps the following illustrations will serve to provide further thought on this subject. In the experiences with the blind boy and girl referred to earlier, both children were ten years old before they could be said to enjoy the custom of exchange of gifts on anniversaries. Up to that time the gift-giving in the family at Christmas time and on birthdays was carefully "arranged" for them in the interests of the other persons involved. Upon occasion both youngsters indicated confusion tinged with resentment at being thanked for presents they had had no inclination to give. So far as receiving gifts was concerned, they were delighted with presents so long as these met exactly the specifications of the item requested. When he was six Marc had liked a large three- wheel trike belonging to another child. He yearned for one exactly like it and was promised that he would be given one for Christmas. The handle bars of the trike found for him differed very slightly in shape from those of his "model" and he could not enjoy it. When asked if he had received what he wanted for Christmas he replied that he had not. The girl at the same age had wanted to be given a toy "standard poodle" with a coat texture which she described over and over again as "not quite stiff, not quite furry." One handling of the one she was given told her that it was a "miniature" not a "standard" poodle and the coat was "felt" to be wrong also. She angrily declared that the dog was not at all what she had wanted and she discarded it as unsatisfactory. During the years from six to ten it was extremely difficult to please either one of these children in gift-giving situations. Ordinarily it is fairly easy, given some knowledge of the child in question, to find an acceptable if not perfect present for the six-year-old seeing youngster. Also, in the case of most children of this age there is a beginning recognition of the giver's intent to please even if he fails to do so. With the two blind children and others like them, the wrong present seems to be interpreted as an insult, lending support to the idea that they retain an excessive degree of egocentricism.

After the age of ten these two children were able to enthusiastically make gifts in school and present them to important people with the usual enjoyment of youngsters when adults lavish praise and appreciation on them for their arts and crafts efforts. However, it was also characteristic of Anne and Marc to insist upon giving to others only an item they themselves liked, regardless of an agemate's or adult's request for a particular thing wanted. By age eight the ordinary child is inclined to begin to select gifts with regard to others' preferences and frequently takes pride in an appropriate selection.

Life experiences in a world largely suited to sighted persons regularly reinforce self-centeredness as new experiences pour in which can only be partially understood because knowledge of their character and meaning usually require visual representation. As the blind child grows older this partial understanding tends to widen the gap between him and his seeing associates. This seems to be a particular problem in latency when, although respectful and curious about differences, true friendships are rooted in similarities and mutuality of viewpoint. It seems as if the blind person, in learning about something new, must regularly return to familiar base—himself—relating all new objects and events to his own context before he can relate them to each other. This idea is a speculation of the writer's based on informal study through teaching and other types of work with young blind children. In attempting to teach concepts of number, size, shape, distance, motion, etc., the children could be readily interested and involved so long as analogies were made to the children's own bodies, personal possessions, or activities. For example, number concepts could be grasped when discussed in terms of the number of fingers, toes, etc.; however, when such concrete knowledge was mastered and manipulation of numbers per se (figuring) was introduced, the traditional difficulties in teaching mathematics to the blind were encountered. The children could speak meaningfully in terms of "how many times" when it referred to their own privileges or "how much" or "many" if it meant food or turns, but beyond their own experiences projection of the concepts of amount, size, distance, etc., became meaningless. This difficulty in the study of mathematics seems to last longer with blind children than with those who are not blind or who do not evidence special difficulty with numbers due to other developmental or perceptual problems. One speculates that a partial reason is that with the self the center of their world they do not relate easily to non-self knowledge.

The blind girl, Anne, was very accurate in recalling numbers when it referred to promises of something she wanted. Also, she was an excellent reporter of events in proper sequence. But she did not like to "put two and two together" even figuratively. At age nine, although she had taken over a measure of responsibility for advancing her own thought processes, she hated to do so and always became angry and sullen when it was suggested "you could figure that out for yourself." "I don't want to hear you say those words again," she would declaim to her teacher who would urge her to "figure." She responded in like manner to her parents in their efforts to break through her self-centeredness and think about *why* people "did what she didn't want them to." She had regularly questioned "Why do they do it when I don't want them to?" truly seeming to wonder why. Her world included little but herself and what was important to her, and her curiosity extended only to events and phenomena relating to herself. A twin sister not blind was able to demand her own rights but at the same time fit herself into the social scheme with markedly less egocentricity.

Marc, at around eleven years of age, revealed that he was only beginning to understand the word "impossible" and to discover that the things and privileges that he had wanted were not deliberately being withheld because someone chose to deprive him. (This included in his fantasy his vision.) The revelation that those who cared for him did not fully control all aspects to his life or their own came through an experience with the natural phenomena of changes in the moon. After spending long evenings trying to "see" the moon with his very faint light perception, he discovered from listening to conversation around him that there were times when the moon could not be seen by people with sight, and further that they had no control over the clouds which could obscure even the full moon. Patiently offered verbal explanations and analogies had simply not convinced him that people couldn't "make things happen" if they only chose to do so. By eleven years of age certain phenomena of nature, both human and otherwise, ordinarily have become a matter of interest and intellectual curiosity to the well equipped, well nurtured child.

After the moon episode, which he referred to as "the night you couldn't see the moon either," Marc kept asking: "What is the universe?" Repeated asking of a question by any child ordinarily indicates that the various responses offered in explanation have still failed to answer it for him. This boy would pursue his line of inquiry with: "Do I live in a universe?" "Well, *where* is it?" "Is this house a 'universe'?" He had responded brightly and fully agreed with someone's comment that he (Marc) wanted to be the center of the universe. The universe' with this boy might be accepted as a confirmation of his high degree of egocentrism. Marc did not share their confusion. He said: "It starts with me." He apparently gained some satisfaction from his involvement with the rather deep subject of the nature of the universe because he suddenly began to show more interest in other people's activities and new knowledge than he ever had before.

The vicarious experiences which could lead to somewhat fuller comprehension of phenomena through reading and through auditory pathways help to extend the horizons of the blind and to enlarge their universe. Marc's curiosity about other people and outer events was stimulated by his interest in learning more about the universe. Although a good Braille reader, he had never read on his own volition. For a time he wanted to read any book so long as it was assured that the word 'universe' appeared in it. He then began to read Braille books for purposes of learning about the weather. This was related to his faint light perception and he hoped to be able to predict the sunny days. As a five-year-old he had had a sad and appealing way of pleading: "Maybe perhaps some day the sun will shine *very* brightly" meaning among many things that the elusive quality to his "light" would no longer trouble him.

Berthold Lowenfeld,[10] in speaking of blindness, is convinced that it is not possible for the blind and the sighted to perceive each other's world. The analogy to "walking in darkness" commonly used to describe what it must be like to be blind does not, according to Lowenfeld, suit the purpose because darkness itself is a visual quality with which the blind have no experience. The closing of the eyes by one who has sight does not call forth a feeling of "blindness" in a blind person's terms because of the presence of recalled mental images. Speculation through such analogies probably serves an important function in inspiring empathic feelings for helplessness in a strange environment, but here it must be recognized that the blind person has available certain accoustic and tactile sensations which help him to feel his way in a strange place. A new place may appear less strange to a blind person than to a sighted person who is blindfolded.

There is a connection, though somewhat indirect, between the inability of the blind and the seeing to comprehend each other's 'universe' and the fact that, although they share a vocabulary, many words reflect experiences differing vastly in character. This refers particularly to the meaning of 'visual' words to the blind. Many individuals who are not blind express surprise at the blind child or adult's free and accurate incorporation of look, see, show, etc., in their vocabularies. In the case of both Anne and Marc it was perfectly clear that visual words made sense to them in their own way of looking at things. However, it was also clear that the boy's slight perception of light caused complications for him to which the girl was not subject. For example, he would sometimes qualify his remarks with "of course, I can't really see it" when he gave something a going over with his hands. Also, he corrected anyone who used the word "light" in a figurative sense such as "beginning to see the light." The girl, on the other hand, would very readily announce "I did see that," if she were handed an object she had already been given a chance to examine. She was curious about the use of the eyes and had at one time said that they were for "tears."[6] At a different time, in a mood of inquiry rather than musing, she had asked if her teacher "was putting her eyes into it" when she knew that the latter was searching for something dropped on the floor. She seemed to assume that the eyes had to be in direct touch with the object being looked for. This was supported by her knowledge that her teacher was bending over. This child, too, had problems of the 'universe' to deal with. With her slowly dawning awareness of a world which she couldn't control and in which all people were not exactly like her, she became interested in the differences which came to light. Her self-centeredness appeared in one of its strongest forms in her insistence that everyone like what she liked. This referred to clothes, records, stories, animals, food, and play themes. It also applied to language. Others were to imitate her expressions and inflections. Her compromise with this was to pretend to be the other person whose manner of speech she then mimicked. She became especially intrigued with words that had a visual reference. She asked about pictures, eyesores (in its figurative sense) scenes, birdseye views, and visions. The last was inspired by hearing *The Night Before Christmas* and she was trying to understand 'visions of sugarplums' as these were said to 'dance through the head.' She thought it must be a "joke" about sugarplums dancing through the head but it must be "serious" about visions dancing. This comment suggested that she experienced some kind of mental fantasy and that she did actually have a concept of a "vision" if not of vision meaning sight. "Insight" was a word that Marc especially loved. He considered it to be the opposite of "outsight" which was what he thought was lacking for him. He said he couldn't see "far enough out."

With both of these children frustration in regard to language was never in relation to failure to understand the conversation of other people. Their true anger was expressed when others failed or refused to understand or agree with them. There were many times in experiences with both children when it seemed quite clear that where the difference was an issue they were angry at others for *not* being blind.

Perhaps more intensive studies of blind persons over a long period of time will reveal more evidence on the subject of the anger felt at those who do not share the blindness. It has been more common to view their problem as one of sadness at loss or deprivation accompanied by a therapeutic attempt to bring light and lightness into their lives in a variety of ways designed to simulate the experiences of the seeing. As co-author of *It Isn't Fair*[4] it has always been a matter of interest to this writer that although the title selected is deliberately explained as applying to the condition of twinship, which the subject so relentlessly resented during her childhood years, many readers either miss or reject the idea. It seems natural to subjectively assume that the title refers to the condition of blindness.

The very real problem of helping blind children to understand and deal with their confused feelings in ways which are constructive to their development suggests the need for psychotherapeutic treatment. The nature of the "pitying" reaction of the majority of people with useful vision to blindness is inclined to support the denial of the problem in the blind as well as the seeing. One questions whether without environmental reinforcement denial would become so popular and ready a defense for a blind person. There is good reason to speculate that the anxiety that must be defended against goes deeper than the sensory defect. In any event, there is much indication that the children in question need help in understanding and dealing with the anger which inevitably accompanies the basic egocentricity and related psychological problems. In both Anne and Marc the state of their mental functioning in the early years was such that at times both autism and retardation were diagnostic considerations. Later, their play, fantasies, dreams, and conversation strongly supported the idea that they wanted to control the world and change others rather than themselves. While Marc played with the idea of increasing the amount of light available to him, he did not complain about blindness or express wishes to be like his seeing age-mates. He and Anne both developed close and satisfying friendships with other blind children which were observed to have a quality of comfortableness that their relationships with sighted children had not. As both children learned to express their anger they improved in their learning. However, the problems created by their self-centeredness and their prolonged dependency contributed to anger to an extraordinary degree. They advanced through temper tantrums, spitting, swearing and name calling to sarcastic remarks as a means of "taking it out" on what they considered to be the source and cause— people who would not do what they wanted. When Anne made up stories or plays, which activity it was hoped would provide her with a more acceptable means of dealing with her feelings against people, these were always around fighting, teasing, punishing, and "going away from." In situations where she felt safe in deliberately making people angry, her genuine satisfaction in having done so was unmistakable.

A group of blind teenagers in a residential situation formed a club in which the password was "The eyes (ayes) have it." That this expressed deeply hostile feelings towards those who were not blind was clear in the 'secret' way in which they let this expression be known. It seemed to be meant to tantalize and challenge those who, by virtue of sight, were not eligible for their 'gang.'

More knowledge of the nature and extent of the problems related to the egocentricity would be of invaluable assistance in planning to provide the many resources needed to meet the special problems of being blind. The root of the problem for the environment is not so much that the blind deplore their sensory defect, but that the environment itself is designed for people who can see.

Summary

There are various studies in process on aspects to ego development in blind persons which shed light on their personality problems. The trend is to focus attention on the effects of this sensory defect on ego formation as it can be observed in the early years of life. This paper suggests that the condition is actively handicapping even in the first weeks because of the significance of the normally equipped newborn's eye contact with the mother in the earliest phase of peripheral vision. It seems that this sight of the baby's eyes following the light and perhaps fleetingly resting on her face is an aspect to the development of this most important relationship.

The problem of the manner in which interpersonal relationships are affected by the lack of visual response is discussed. Special emphasis is given to the high degree of egocentricity which is commonly said to be a continuing characteristic of blind persons. This should be accepted as an aspect to the sensory defect rather than a problem of adjustment. The blind person's individual adjustment to getting along with others who are not blind should be healthier if his self-insight includes knowledge of the deeper roots of the need to manipulate others and maintain excessive self-interest. The anger at others resulting from the egocentricity creates an enormous problem for all concerned. This can have an effect on the development of the learning skills because of the likelihood of an accompanying depression.

Psychological problems are inevitable, indicating clearly the value of psychological support for the mothers of blind babies and also of psychotherapy and/or psychoanalysis for the child as he advances in years.

In the interests of helping blind persons to develop and use their resources as fully as possible, it is important that study of and attention to the psychological problems keep up with the advances in development of aids to their educational and vocational life. Physicians who identify blindness in the early weeks can make a generous contribution to knowledge both by their observations and their guidance of the mother in her handling of her baby.

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The Power of Prophesy

No man is a true prophet otherwise than through the possession of such intimate knowledge of a subject that he is able to say, "Thus matters must develop." Such was Claude Bernard's prophecy of the future of his own science. His understanding of physiology had become so perfect that the future could not be wholly doubtful. He knew where the path must lead.—L. J. Henderson. Introduction. Claude Bernard, M.D. *The Introduction to the Study of Experimental Medicine*. New York, The Macmillan Company, 1927, p. ix.

CHILD DEVELOPMENT AND SCIENTIFIC VALUES

Albert J. Solnit, M.D.

In examining the topic "Childhood and the Two Cultures," it is fitting that we look at ourselves collectively and individually. Perhaps this perspective is especially pertinent because the Yale Child Study Center has been a demonstration that in Connecticut, in New England, the cradle of our country we have a tradition of concern about our greatest resource, our children. It is not at all unusual to find a consensus about the primary worth which we attribute to children, but it is somewhat unusual to see such words matched by deeds. I am reminded of a story by Lafcadio Hearn.[1] On Hearn's first day in Japan he was taken on a tour of a Buddist temple. The priest led him from one room to another and still to another. At last they reached the altar in the innermost room, and there Hearn saw the end of his quest—a mirror; himself. When a group agrees to concern itself with the study and care of children, the past and future of our society will always be at the center of their attention. Childhood is at once the past out of which the future develops and the present from which there can be no turning back if we are to gain a brave new world.

As we look in the mirrors of the past and future, perhaps we should seek the illuminations that are sharpened and enriched by contrasts. Childhood can be viewed as a study of two cultures—that of the child and that of the adult; that of the past-present and that of the present-future. There are, after all, two sides to the present, one that faces to the past, history's gift, and one that faces to the future. There are other contrasts: that of the boy compared to the girl in our society; those contrasts of different ethnic and cultural groups such as that of the Negro American child and that of the White American child. In addition, one can view the contrasts of the child asleep and the child awake; the privileged compared to the disadvantaged child; and the contrasts between the younger child and the adolescent. In the last contrast you will also recognize the continuum that connects the extremes, which is true of each of the above polarities that I have suggested.

As we look in our mirror you will note a tendency that expresses a slightly reproachful and bitter interpretation and emphasis. This issue of *Connecticut Medicine,* one which is in the service of children, provides an opportunity for us to see where we have failed children, and thus ourselves; for were we not children once ourselves? We have not succeeded in demonstrating our professed priorities for children. Children do not have effective champions—they lack for militant lobbyists. Everyone speaks for them but usually in the service of the adult's image. Let us look at our mirror with an emphasis on what it suggests about the past and future of children and of the children from whom we developed.

In the scholarly book, *Centuries of Childhood*[2], Phillipe Aries states:

> "In medieval society the idea of childhood did not exist; this is not to suggest that children were neglected, forsaken or despised. The idea of childhood is not to be confused with affection for children; it corresponds to an awareness of the particular nature of childhood, that particular nature which distinguishes the child from the adult, even the young adult. In medieval society this awareness was lacking. That is why, as soon as the child could live without the constant solicitude of his mother, his nanny or his cradle-rocker, he belonged to adult society" . . . "Language did not give the word 'child' the restricted meaning we give it today; people said 'child' much as we say 'lad' in everyday speech" . . . "The infant who was too fragile as yet to take part in the life of adults simply 'did not count'; . . . (an) expression used by Moliere, who bears witness to the survival in the seventeenth century of a very old attitude of mind."

Loren Eiseley, distinguished American anthropologist, indicated his view of a child's two worlds[3] as follows:

> "When I was a small boy I lived, more than most children, in two worlds. One was dark, hidden and self-examining, though in its own way not without compensations. The other world in which I somehow also managed to exist was ex-

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A modified version of this article was presented at the University of Florida in March 1967 on the occasion of the dedication of the first phase of a Human Development Center, the Children's Mental Health Unit and the Developmental Research Unit.

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ternal, boisterous, and what I suppose the average parent would call normal or extroverted. These two worlds simultaneously existing in one growing brain had in them something of the dichotomy present in the actual universe where one finds behind the ridiculous, wonderful tent-show of woodpeckers, giraffes, and hoptoads, some kind of dark, brooding, but creative void out of which these things emerge—some anti-matter universe, some web of dark tensions running beneath and creating the superficial show of form that so delights us. If I develop this little story of a personal experience as a kind of parable, it is because I believe that in one way or another we mirror in ourselves the universe with all its dark vacuity and also its simultaneous urge to create anew, in each generation, the beauty and the terror of our mortal existence."

In contrast to the modern introspective observer, an observing philosopher of our past, Rousseau[4] in his classic *Emile* said:

> "Nature wants children to be children before they are men. If we deliberately pervert this order, we shall get premature fruits which are neither ripe nor well-flavoured, and which soon decay. . . . Childhood has ways of seeing, thinking, and feeling peculiar to itself; nothing can be more foolish than to substitute our ways for them." . . . "They are always looking for the man in the child, without considering what he is before he becomes a man."

As these quotations indicate, I believe we shall see a more useful image in our mirror if we are able to see that in the study of childhood and of children the separation of science and the humanities takes place at great risk to ethical as well as scientific and literary considerations.

C. P. Snow has captured our imagination with one view of the threatening human dilemma represented by the gulf between man's self represented by the humanities and man's self represented by the sciences and their technologies. This split in man can be likened to the splitting of an atom and the fearsome or wonderful possibilities presented by the availability of such energies. Children, their understanding and care, make us sharply aware of our destructive impact when scientific study is viewed as independent of humanitarian considerations in their care. In his essay, *The Two Cultures and a Second Look,*[5] Snow has stated:

> "In our society (that is, advanced western society) we have lost even the pretense of a common culture. Persons educated with the greatest intensity we know can no longer communicate with each other on the plane of their major intellectual concern. This is serious for our creative, intellectual and, above all, our moral life. It is leading us to interpret the past wrongly, to misjudge the present and to deny our hopes of the future. It is making it difficult or impossible for us to take action."

In his essay Snow indicates that the most pointed example of this threatening gulf is that between scientists and the literary intellectuals. Of course, by "culture" Snow refers to the development of the mind as well as to the definition that refers to the anthropological concept of a group of persons living in the same environment, linked by common assumptions, traditions and a common way of life.

Our dilemma is brilliantly caricatured in the vision of a tormented literary giant of the last century. In *The Brothers Karamazov*[6], Dostoyevsky says:

> "That's exactly the same sort of thing a doctor told me a long time ago . . . he was an elderly and undoubtedly clever man. He spoke to me as frankly as you, though in jest, but in mournful jest. 'I love humanity,' he said, 'but I can't help being surprised at myself; the more I love humanity in general, the less I love men in particular, I mean separately, as separate individuals. In my dreams I am very often passionately determined to serve humanity and I might quite likely have sacrificed my life for my fellow-creatures, if for some reason it had been suddenly demanded of me, and yet I'm quite incapable of living with anyone in one room for two days together, and I know that from experience. As soon as anyone comes close to me, his personality begins to oppress my vanity and restrict my freedom. I'm capable of hating the best men in twenty-four hours; one because he sits too long over his dinner, another because he has a cold in the head and keeps on blowing his nose. I become an enemy of people the moment they come close to me. But, on the other hand, it invariably happened that the more I hated men individually, the more ardent became my love for humanity.' "

Our rapidly developing dilemma is equally threatening in medicine when one considers the widening gap between the complex demands for continuous humane care for all patients and the demands that the modern physician acquire the most advanced technical skill and knowledge of the biological and psychological sciences.

This crisis apparent in medicine is a threatening general condition in terms of the gap between the sciences and the humane letters and arts. Man's extraordinary capacity for specialization has burst out of the mold in which coordination and synthesis of knowledge and services can occur. An awareness that we are faced with an explosion of knowledge and technology becomes more dramatic when we realize that much of biological and medical knowledge becomes obsolete in about 10 years and that this trend is accelerating. As the differentiation and fractionation of techniques and knowledge, i.e. specialization, has permitted us to reach understanding in depth, our capacity to correlate and coordinate our labors and achievements has sunk to a dangerously low level. Specialization without synthesis is a threat to our society since the destructive forces in any particular field, especially in the physical sciences, are frequently unleashed when they are not bound to the knowledge and techniques of the other institutionalized endeavors of our society which permit us to be characterized as a civilization. There is a competition amongst the apparently unrelated fields. This divergence that appears to be necessary for the concentration that produces new understanding in one special area has been accompanied by a relative fall in the quality of integration of knowledge essential for the survival and development of a democratic society.

The study of children cannot be separated from the care of children without greatly risking advances in our knowledge, the desperate need to which this Center testifies. Biochemical and molecular biological advances in our understanding of children are of critical importance especially the breakthroughs that will bring crucial assistance to psychotic and retarded children and their families; increased knowledge that will strengthen our effectiveness in the areas of congenital and genetically transmitted defects, malignancies and metabolic disorders of childhood; and in the more effective prevention and treatment of deficiency conditions and infectious and parasitic diseases for the children of the underdeveloped countries of the world.

However, the greatest number of children at risk in all countries are those who are deprived of the best knowledge we have available to protect and promote their sound and balanced development. When we realize that emotional deprivation, accidents, abuse, and discontinuities of protection, affection and stimulation are the greatest threats to the developing child in the country today, we can well understand why this Center needs to be elaborated and supported without reservation. Such centers must be multiplied throughout the country. We can also realize that the culture of the humanities and the culture of the sciences must be integrated and coordinated—this gulf must be obliterated if we are to study and care for children effectively and creatively. The humanities can remind us in compelling universal terms of our priorities and describe the humane setting which we and our children should strive to create. A poem, a literary essay, a short story or a novel may, through virtuosity, reveal our human condition, raise the voice of the child and project the dreams on which a better world can be offered to our children. Perhaps the best offering of our civilization is the music and poetry it has created—the transformed gifts of man's inner world to his social world. The ascent of Everest and space travel are magnificent human achievements, but they border on destructiveness, alienation and nullity unless these achievements are balanced by the social meaning they acquire as extensions of the human ethical values and range of experiences represented by democratic ideals, humanitarian practices, and the aesthetic expressions of which man is capable such as poetry, music, dancing, and the large variety of literary and art forms of creativity. We have become a society in danger of serving the sciences rather than being served by them. We believe science can give us the power to control our physical environment and to improve things, not people. ". . . man's increasing technological know-how encourages a separation between our tools and our knowledge . . . the tools that man makes, make man." In a recent symposium[7] at which this statement was made, learned theologists, scientists and scholars in the letters and arts addressed themselves to "The Shape of the Future." A thoughtful series of dialogues, this symposium revealed, by omission, the problem to which I am addressing myself. In discussing "The Shape of the Future," there was no one to speak for the children of the present or the future.

The scientific action-study of children is one of the crucial bridges between the humanities and the sciences. This awareness has been carefully avoided in recent dialogues concerning the failure of our humanistic and scientific cultures to develop an influential and world-saving dialogue. Scientists and technologists want to avoid the diffusion and distractions they fear will obstruct the intense and specialized magnifications of their research focus. Humanists are fearful that the scientist-technologists are dehumanizing our society and transforming our planet into a place unfit for man and his civilized selves.

The study and care of children require that scientific and humanistic concerns be joined since the most important problems which threaten our children cannot be well exposed, thoroughly understood and courageously prevented and treated unless we are able to study them in the context of interventions. These interventions are those characterized as action-research, but in a certain sense all research has an action component which influences what is being observed. The Heisenberg principle of indeterminacy states this with parsimonious elegance. Assuming that the aim of science is to understand man and the worlds he perceives and infers, we test science through making predictions. Of course, accurate predictions may be impossible. Forty years ago Heisenberg, a nuclear physicist, formulated the "uncertainty principle" or the "principle of indeterminacy" which states that the process of observing alters the data that is being collected. The more accurately one tries to observe, the more likely it is that the observer will modify or change what is being observed.

Translated into terms of clinical action-research, the act of rendering a service, an essential variable in such research, makes possible the continuity of observation and provides access to relevant data in child development which otherwise will be missed. In such studies psychiatric, pediatric, educational, psychological and social work services are often provided, and the investigator must be prepared to act within the field of his observation. He becomes, as it were, a part of the field or the process which he studies. This requires that precautionary measures be taken to protect the validity of the data through being able to describe the distortions created by the services rendered and by the observational process. Thus, the clinical action-research method unifies scientific aims and social needs which Centers such as this will serve in its training, research and service activities.

The children in our society at greatest risk and therefore in greatest need of service-oriented action-research are those who are born out of wedlock, those who live in institutions, those who have accidents in early childhood, and those who fail to thrive due to neglect, abuse or a choatic and deprived life-situation. Official statistics that are indices of these "happenings" represent but a fraction of the estimated children suffering from these conditions. Some of these statistics are:

1. In 1962 it was estimated that there were at least 60,000,000 children under 14 years of age, making up approximately 30 percent of the total United States population. According to the most conservative estimates, over 2,500,000 of these children, not including preschool children are in manifest need of psychiatric evaluation and treatment.
2. In 1959, 265,000 children between the ages of seven and seventeen were presented to juvenile courts on petitions of neglect and delinquencies.
3. In 1960, according to the U.S. Census of Population, there were more than 15,000 children under the age of five years in institutions in this country.
4. There are almost two million adopted children under 18 years of age in the United States today (Children's Bureau of the Department of Health, Education, and Welfare). Each year more than 140,000 children are adopted in the United States. Most of these children are born out-of-wedlock. The best estimates indicate that only one-third of the total children born out-of-wedlock are adopted.
5. In 1962, according to the National Health Survey (National Clearing House for Poison Control Centers, 1962), over 400,000 children a year were seen by physicians for accidental poisoning.

Our most critical challenge is that of responding preventively and therapeutically to the threatening and devastating corrosion of the life development of these children. Such corrosion often has a permanent scarring and depleting effect upon the mental and emotional development of these children who lack adequate and continuous care and stimulation.[8] These children become blighted by the way they are reared or exposed without safeguards to the adult world. We have failed to create a world satisfactory for the full and rich development of the healthy, potentially creative child. Rather we have succeeded in promoting the development of the child who functions at a retarded level and who is confused by our peaceful democratic intentions and our discriminatory war-like postures. We must have the resources to intervene. Through the study and evaluation of what is illuminated by these selected and humanistically based interventions, child psychiatrists, pediatricians and their colleagues in education, nursing, social work and psychology, as well as the new professions, will provide crucial strength, knowledge and leadership in narrowing the credibility gap between what we want for our children—our future world—and what we have provided so far for our children. Excellent centers for children, if properly supported, can fructify clinical scientific engagements in service-oriented action-research and can provide new models for the preventive and therapeutic care of children.

As an example of the perspectives revealed by such avenues of research, we have gradually accumulated evidence that suggests a condition I term the depleted mother syndrome. In our studies of infants who fail to thrive,[9] toddlers who accidentally ingest poison[10], the abused and neglected child[11] and older children who suffer accidental fractures of their limbs, we have become aware that one red thread in that fabric of human suffering is the mother's inability to thrive—the negative balance between her resources and the demands made by her family and life situation. So often the mother's suffering and the consequences of accumulated neglect of her needs are only revealed when one establishes a responsible but non-judgmental alliance with her to understand what has happened and to offer assistance that enables the mother and father to protect more effectively and more satisfactorily the joyous and healthy development of their children.

Life in our industrialized urban society often has a variety of ways, subtle and obvious, of depleting the energies and satisfactions of the parents, especially the mothers, of young children. Parents cannot nourish and protect their children emotionally and psychologically if they suffer from a deficiency of emotional supplies for themselves. These defficiencies may accrue from past deprivations and traumatic experiences, present inadequacies of support and satisfactions, and future hopelessness. Enabling the mother to restore her energies and to regain her positive motivation requires interventions such as homemaker services, social work assistance for the parents, pediatric, psychiatric and nursing care for the child and the mobilization of appropriate family and community resources. Restoring the man to his function as husband and father will require us to provide him with assistance to find and use work opportunities that enable him to achieve self-esteem as a man who can expect his wife and children to feel affectionately proud of him. Learning to work and earning a living are complex functions that evolve gradually. Our welfare system will need to move rapidly toward encouraging such a development while the man lives with his family, rather than to shut off welfare assistance at such a time. Through learning and earning a man can view burning as an unnecessary and destructive alternative. These interventions must be evaluated critically if we are to advance our knowledge about children and our capacities to provide effective opportunity-services for children and their families.

Action-studies, service-oriented investigations permit us to become aware of interventions that represent our best available knowledge designed to relieve and prevent such conditions. Our research sophistication enables us to evaluate these interventions in order to modify or refine them. Heuristically, such clinical research is crucial as a source of theory construction necessary to advance our knowledge conceptually as well as practically.

Thus, we can see that a split between research and intervention, between scientific and humanistic considerations is artificial, interfering both with the acquisition of knowledge and its practical applications. Children will benefit if we can realize that the early models of scientific research in the laboratory have a continuing, though limited, usefulness in certain important areas of chemistry, physics, physiology and genetics as related to human biology; but the study of man as a complex, developing, adapting social organism also must exploit and update the naturalistic models of Darwin and Freud if we are to avoid the errors of simplistic study. Through such studies we can make maximum usefulness of man's capacity to observe more pertinently and with greater illumination when he is in "the field" where the distortions, consonant with his social needs and expectations can be taken into account in the evaluation process. Thus, it is through the concern for children and knowledge about children that we can see clearly that there is no need to feel trapped by what is a pseudo conflict between scientific and humanistic cultures—between science and art. Both of these human ventures and expressions can be joined harmoniously as enlightened allies in the best interests of the child and adult.

Our state and region can accept leadership responsibilities in putting science in the service of a better world for all children, and can commit itself to the full elaboration of these efforts and services.

In his poem "The Gift Outright" Robert Frost has expressed well what our intentions could be:

> "New order of the ages" did we say?
> If it looks none too orderly today,
> 'Tis a confusion it was ours to start
> So in it have to take courageous part.*

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* From "For John F. Kennedy His Inauguration" from *In The Clearing* by Robert Frost. Copyright © 1961, 1962 by Robert Frost (Holt, Rinehart and Winston, Inc., New York). men." In Yale Symposium, "The Shape of the Future,"

What to Expect of Life

Do not begin life with expecting too much of it. No one can avoid his share of its anxieties and difficulties. You will see persons who seem to enjoy such advantages of birth and fortune that they can have no difficulties to contend with; and some one of you may be tempted to exclaim, "How much is their lot to be perferred to mine!" A moderate experience of the world will teach you not to be deceived by these false appearances. They have not your difficulties, but they have their own; and those in whose path no real difficulties are placed will make difficulties for themselves . . . There is no great happiness in life than that of surmounting difficulties; and nothing will conduce more than this to improve your intellectual faculties, or to make you satisfied with the situation which you have attained in life, whatever it may be.—Holmes, T.: *Sir Benjamin Collins Brodie, London,* 1898.

THE PRESIDENT'S PAGE

Not long ago I attended the Annual Convention of the American Medical Association in San Francisco. It is a pity that more doctors do not interest themselves in the meetings of the House of Delegates since these meetings are open to all members. You need not be a delegate to appear before the various reference committees of the House. In fact, the majority of people who speak or appear are not delegates. Since most of the work of the convention is done in reference committees, those members who appear before them are actively taking part in the affairs of organized medicine. This is the right of each doctor. This is, of course, impractical each time the House meets, but each physician should participate as often as possible. A fellow physician once said to me, "Why should I belong to the American Medical Association? What has it done for me?" How can such a question be answered? I remarked that it probably would be difficult to justify membership to anyone who felt it important to ask such a question.

The American Medical Association was founded with the avowed intention of improving and standardizing medical education in the United States of America. Medical education had become in many instances very poor, and the doctors of the country decided to remedy what they knew was a serious situation. It took a good deal of effort to start such an organization. There was much opposition. You might be surprised to hear the names of some of the medical schools which actively resisted any attempt to make them change their ways. This does not sound like an organization being founded to further the ends of the medical profession. Indeed, it sounds rather like the formation of an association dedicated to the betterment of medical knowledge and care. Even in these times, ninety-five percent of the work of the American Medical Association is devoted to scientific matters. This is something that most of its members do not know. Unfortunately, many doctors still make their estimate of the American Medical Association by what they read and hear from those in no way associated with it. How much better it would be if a personal investigation were made instead!

The doctors of the country should be proud of what has been done to better medical education and improve the health of the people. It is no accident that we have the best medical care in the world. It is the result of steady effort on the part of organized medicine.

The American Medical Association needs and deserves your active support. It is the best hope we have for the continuation of medical progress. If it is to succeed now as it has in the past, it must have the deep interest of every doctor.

Let's move ahead.

Norman H. Gardner, M.D.

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Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

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Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

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Josephine P. Lindquist
Assistant to General Manager

SUMMARY OF ACTIONS COUNCIL MEETING
Thursday, June 27, 1968

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Caplan, Grendon, Weber, Brandon, Abbot, Fabro, Bradley, Rogol, Cramer, Egan, Petrie, Purnell, Shepard, J. M. Grant, Nemoitin, Johnson, Friedberg, McDonald, R. F. Grant, Pelz, Granoff and Roch.

Also present were: Mrs. Lindquist, Mr. Villano, Mr. Norbeck (AMA), Dr. John W. Patterson, Dean of the UConn Medical School, and Dr. Richards.

Absent were: Drs. Farrell, Spitz, Wilson and Palomba.

II. ROUTINE BUSINESS

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Milton R. Arons, Hartford (HCMA)—1968
Louis F. Meister, Falls Village (LCMA)—1968

Resignations and Appointments

(a) *Delegate to the Maine Medical Association:* It was VOTED to elect Charles Polivy, Hartford, to this post to replace Payson B. Ayres, Greenwich, resigned. In the event that Dr. Polivy cannot accept the appointment, Bernard O. Nemoitin, Stamford, is to be asked to serve.

(b) *Conference Committee with State Bar Association:* It was VOTED to accept with regret and thanks for past service, the resignation of Averill A. Liebow, New Haven (now of California), as a member of this Committee.

(c) *Committee to Study Perinatal Morbidity and Mortality:* It was VOTED to accept with regret the resignation of Marcus E. Cox, Waterbury, as a member of this Committee. The question of appointing a replacement for Dr. Cox on the Committee is optional and was left open.

(d) *Committee on Postgraduate Education:* It was VOTED to accept with regret the resignation of John J. Kneisel, Hartford, as a member of this Committee, and it was further VOTED to appoint Daniel Marshall, Hartford, to replace Dr. Kneisel as a member for the balance of the latter's term.

Date of Next Meeting

The date for the next meeting of the Council was set for Wednesday, July 24, 1968. To the fullest extent possible, this meeting will be devoted principally to the report of the Ad Hoc Committee on CRMP Grant Request.

III. OLD, NEW AND SPECIAL BUSINESS

Introductions

The Chairman introduced and welcomed Isadore H. Friedberg, Newington, as the newly-appointed Associate Councilor from the Hartford Association. The Chairman also welcomed John W. Patterson, Hartford, Dean of the UConn Medical School, who expressed his pleasure at being invited to join the Council at this and subsequent meetings and, later, participated in the discussions of several items of business on the agenda.

Presentation

On behalf of the Council, and with appropriate accompanying remarks, Norman H. Gardner, President, presented Stevens J. Martin, Chairman, with an inscribed gavel which expressed thanks and appreciation to Dr. Martin for his capable and dedicated service as Chairman, 1963-1968. In accepting, Dr. Martin responded with similar expressions of thanks and appreciation for the help and cooperation given him by members of the Council during the past five years of his Chairmanship.

Report—Delegate to MSNJ

It was VOTED to accept a report filed by E. Tremain Bradley, Delegate to the Medical Society of New Jersey, on his attendance at the MSNJ Annual Meeting, May 18-21, 1968. It was further VOTED to refer a section of the report dealing with procedure for nominating committees to the Committee on Preliminary Study of Nominations, as information, and to the Subcommittee to Study and Revise the Bylaws, for study and report.

Report—Delegate to MMS

It was VOTED to accept with commendation, a report filed by Max Caplan, Delegate to the Massachusetts Medical Society, on his attendance at the annual meeting of the MMS Council (House of Delegates), May 20, 1968. It was further VOTED: (a) to refer a section of the report dealing with professional courtesy in relation to third party payors to the Judicial Committee for study and report; and (b), to refer a section of the report dealing with protection against suit for physicians serving on Utilization Review Committees, either by legal statute or through appropriate liability insurance, to the Committee on Hospitals for study and report.

Report—Representative to 2nd National Congress on Socio-Economics of Health Care

It was VOTED to accept with commendation, a report filed by James H. Root, Jr., Waterbury, on the proceedings of this National Congress, Chicago, March 22-23, 1968, which he attended as a representative of the Society. It was further VOTED to request the Chairman to appoint an appropriate ad hoc committee to study and report on the definition of group practice, the various types of groups, the methods of financing, the quality of care furnished, the cost, etc., such report, when finalized, to be publicized as information to the membership.

Report on "Tri-State" vs. "CUPISS" Data System Proposals

It was VOTED to accept with thanks a report filed by Carl W. Johnson, Thompsonville, and Isadore H. Friedberg, Newington, on a meeting held with Commissioner Franklin M. Foote on April 29, 1968, at which the so-called "Tri-State Plan" (Health Resources and Information System for Coordinated Planning and Management) being advanced by the State and the "CUPISS" plan (Connecticut Utilization and Patient Information Statistical System) of the Regional Medical Program were compared, contrasted and defined as to their respective objectives and jurisdictions. Pursuant to the acceptance of this report, it was VOTED to request the Chairman to appoint a qualified CSMS member to serve with the technical advisory committee to the CUPISS study group of CRMP.

Report—Representative to 3rd National Conference on Health Education of Public

It was VOTED to accept as information the report filed by Peter F. Villano, PR Director, on the proceedings of the Conference, Chicago, April 4-6, 1968, which he attended as a representative of the Society. It was further VOTED to send copies of the report, with pertinent sections appropriately marked, to the following:

(a) *Presidents of Yale University and UConn:* Sections on university health services and health education programs at the college level.
(b) *CSMS Committee on Hospitals:* Sections on health education of patients as a function of hospitals.
(c) *Commissioner of Higher Education:* Sections on health education programs at all levels of higher education, as follow-up to basic programs of health instruction "from kindergarten through high school".

Election of Judicial Committee

It was VOTED to accept the report of the Committee on Preliminary Study of Nominations on nominations for the newly-established (5/1/68) Judicial Committee, and to elect the slate presented as follows:

County Members (8)

County	*Name*	*Term*
FCMA	Milton M. Lieberthal, Bridgeport	1968-69
HCMA	Reginald C. Edson, West Hartford	1968-72
LCMA	J. Alfred Fabro, Torrington (Chairman)	1968-72
MCMA	Archibald W. Thomson, Jr., Middletown	1968-71
NHCMA	Clyde L. Deming, New Haven	1968-70
NLCMA	Nicholas T. Phillips, Norwich	1968-70
TCMA	David S. Hastings, Stafford Springs	1968-71
WCMA	William Mac Shepard, Putnam	1968-69
	At-Large Members (4)	
MCMA	John R. Egan, Old Saybrook	1968-69
FCMA	Louis Rogol, Danbury	1968-70
NHCMA	Orvan W. Hess, New Haven	1968-71
WCMA	Ralph L. Gilman, Storrs	1968-72

Report—Committee on Postgraduate Education

It was VOTED to receive as information a report filed by Vincent A. DeLuca, Jr., Chairman of the subcommittee of the Committee on Postgraduate Education, concerning the success of the project to publish regularly in the Journal a listing of educational meetings throughout the state which are open to all members of the Society. It was further VOTED to extend indefinitely the original six-months trial period for the project, it being noted that no additional funds would be required to implement same "for another full year."

Report—Committee on Awards for CSMS Service

It was VOTED to accept the report filed by the Committee which, in brief, recommended that appropriately inscribed certificates of service be awarded to County Councilors (and/or Associate Councilors) upon their retirement from office at the end of one or more terms; that the Incoming President be given an inscribed gavel at the time of his inauguaration; that the Retiring President, in addition to the Past President's Pin, be presented with an inscribed silver bowl at the end of his year in office; and that other CSMS officers, upon retiring from an office after one or more terms (excluding the President-Elect and Vice-President) also be given an inscribed silver bowl. It was further VOTED that the silver bowls should be made of sterling silver, and the effective date of this awards program be 1966 (Annual Meeting dates).

Legislative Position on Therapeutic Abortion

In response to a request for direction received from the Committee on State Legislation, regarding legislative activities to be undertaken by the Society re therapeutic abortion at the 1969 General Assembly, it was VOTED to reaffirm support of the statement on this subject adopted by the CSMS House of Delegates on May 1, 1968, and urge the Committee on State Legislation to confer with other groups who are interested in revising the current statutes on therapeutic abortion for the purpose of seeking support for the Society's position on same. Also asked by the Committee, but not answered by the Council at this meeting, was the question of whether the Society should have its own bill on statute revisions introduced or limit its activities to supporting or opposing bills introduced by others.

Communications—New Haven County Medical Association

(a) The Board of Governors of NHCMA referred to the Council for study and opinion an instance in which a judge of a Superior Court handed down a decision in which he found the charges of an attending physician "a bit high" and distributed copies of the decision to all parties to the case and made it public (in open court). The NHCMA Board found the physician's charges "very modest" and feels that some protection should be offered to a physician under such circumstances; that the judge should certainly have asked for a review of the charges by the county medical association before passing personal judgment of them in his decision and to the public. It was VOTED to refer this problem, with all pertinent background materials, to the Conference Committee with the State Bar Association for study and report. A secondary point of issue (under a 1967 statute) was the ruling of the judge that witness fees of several physicians who testified in the case could not exceed the total amounts of their bills for professional services rendered to the patient.

(b) The NHCMA Board also referred to the Council for evaluation a proposal of a member that, under proper licensing authority, minor surgical facilities for short-term inpatient care could be developed which would (1) relieve the bed shortage in general hospitals, and (2) provide adequate equipment and personnel for minor surgery at lower cost. Hopefully, if approved by the State Health Department, such facilities would be eligible to receive payments from Blue Cross and other third parties. It was VOTED to refer this proposal to the Committee on Hospitals for study and report to the Council.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on June 27, 1968. Detailed minutes of the meeting are in file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

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Special Article

BEHAVIORAL TOXICITY OF PSYCHOTROPIC DRUGS: I. DEFINITION II. TOXIC EFFECTS ON PSYCHOMOTOR FUNCTIONS

Alberto DiMascio, Ph.D., and Richard I. Shader, M.D.

I. Definition

Psychotropic drugs may beneficially affect the behavior of mentally or emotionally disturbed individuals. They may also, however, alter behavior in ways which are deleterious to the person. This latter phenomenon has been called "behavioral toxicity"[1], a term which has been so relatively recently coined that a definition of what it encompasses, or excludes, has yet to be firmly established.

To Cole[2], upon whom first fell the task of describing this phrase as it applied to humans, "behavioral toxicity" included those "adverse" subjective mood changes and "decrements in objective performance" that result from drug ingestion. This description included both those behavioral changes resulting from the drug and—although not specifically indicated—those changes in response to the perception of non-behavioral effects such as "akathisia" and the "parkinsonian syndrome". Fingl and Woodbury[3] subsequently defined the term as including the ". . . suppression of normal anxiety, reduction in motivation, impairment of memory and learning, distortion of judgment, impairment of reflexes, motor incoordination, non-purposive or inappropriate behavior, and other adverse effects of drugs on mood, behavior, and psychological and psychometric functioning." Holliday[4], has pointed out that ". . . there is probably nothing listed outside of the realm of behavioral toxicity by Fingl and and Woodbury that, *in the sense the term is used by Cole*, does not interfer with behavior." She amplifies on this by pointing out that in using this broad definition" . . . one's behavior could be said to be affected either directly or indirectly if one were suffering from drug allergies, a blood dyscrasia, a blood dyscrasia, hepatotoxicity or nephrotoxicity. . . ." It seems obvious from the above that a meaningful definition of "behavioral toxicity" must include only those changes that cannot be traced to some direct or immediately specificable antecedent biochemical or physiological effect of a drug.

Germaine to the definition are the implications of the words "toxicity" and "side-effects". These terms are highly relative ones that have meaning only in reference to the setting in which a drug is used or in which the observation has been made; a value judgment is basic to both terms. "Toxicity" and "side-effects", as they have been conventionally used, imply an action that is both *adverse* to the health of an organism and *undesirable* in regards to the use for which the drug has been employed. The tendency has been to select, from among the many pharmacologic actions that a drug may possess, a specific effect to consider as the main (therapeutic or beneficial) effect and to describe all others as side-effects.

In physical medicine it is usually possible to direct one's attention to a given objectively determinable end-point, and to specify the desired "main beneficial effect" of a drug. Further, whether they occur to drugs used in physical medicine or in psychiatry, when "organic" toxic effects to a drug are noted—such as a blood dycrasia, liver necrosis, peripheral neuropathy, paralytic ileus, etc.—there is no argument that they are both adverse and undesirable. Such is not always the case with respect to the many effects encompassed under the term "behavioral toxicity" or "behavioral side-effects".

In psychiatry there is often no clearly specifiable endpoint (the behavior that we wish to alter being so global or the phenomena encompassed so varied, e.g., psychosis, schizophrenia, depression—that they almost defy objectification) by means of which we can point to the "main therapeutic" actions of a drug. Nor can we consistently point to some of the behavioral changes the drugs induced and the state that these clearly are adverse and undesirable.

A drug effect (e.g., sedation, motor stimulation,

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mood suppression, slowing of mental processes, etc.) may be considered adverse for one patient yet therapeutic and desired for another patient; may be of value in the treatment of a given patient at one stage of his illness and adverse at a later stage, and may be produced or noted in some patients and not in others—indeed, the same drug may induce the opposite effect in still other patients.

In spite of the confusion and problems arising from the above, an attempt will be made to set some limits for the scope of the topic within which a definition may be presented and within the available findings may be summarized.

To our way of thinking, Fingl and Woodbury's definition of "behavioral toxicity" is sufficiently descriptive of the types of human functioning encompassed, and it actually could be *sufficiently exclusive,* if the restriction were made that only those changes in these functions *resulting from direct pharmacological action* are to be discussed under this heading. Those behavioral changes that are reactions to immediately specifiable antecedent biochemical or neurophysiological effects of a drug are not appropriate for inclusion. The concept of "behavioral toxicity" may thus be viewed as a wastebasket category in which to place many of the actions of a drug that presently cannot be understood in terms of specific pathways or levels. The scope of what is included under this heading will progressively diminish, as we are able to specify more and more the biochemical or neurophysiological determinants of a given behavior (e.g., mental retardation was considered a global behavioral phenomenon or abnormality until phenylketonuria (PKU) and other inborn errors of metabolism were recognized. Now these types of mental retardation are considered to be biochemical phenomena—with behavioral consequences).

Dosage of drug administration is related in a presently inextricable way to the incidence and/or severity of drug-induced changes. Implicit in most discussions of "behavioral toxicity" or "behavioral side-effects" is the tacit agreement that until more facts are available little mention be made of dosage phenomena. If a change is produced that is considered a "behavioral side-effect"—at any point along the dosage continuum, it may be included without specifying the dose at which it was noted. This is probably done in order to avoid the presently unfathomable "thresholds of emergence" problem. It is further agreed—and fittingly so—to include only those drug-induced changes that occur at some point within the usual therapeutic dosage range. With full cognizance of the possible problems this may pose, we shall adhere to these agreements.

Finally, to be include in any discussion of "behavioral toxicity", a drug-induced change should be as universally as possible agreed to as adverse or undesirable, regardless of the therapeutic intent in administering the drug. Accordingly, "sedation" would not be included under the term, while "excessive sedation" would; "mood dampening" would not be included, but "depression-inducing" would. This restriction, because it inherently involves the assessment of the degree or intensity of impairment resulting from the change induced, in addition to judgment of the value of said change, is the most problematic.

The definition of "behavioral toxicity" at which we arrive is as follows:

> "Behavioral toxicity" is a phrase used to denote those pharmacological actions of a drug that, when administered within the dosage range in which it has been found to possess clinical utility, produce—through mechanisms not immediately specifiable—alterations in perceptual and cognitive functions, psychomotor performance, motivation, mood, interpersonal relationships, or intraphyschic processes of an individual to the degree that they interfere with or limit the capacity of the individual to function within his setting or constitute a hazard to his physical well-being.

The material to be covered in this and subsequent presentations will be restricted to those drugs of primary therapeutic import in clinical psychiatry—the antipsychotic, antidepressant and antianxiety drugs.

II. Toxic Effects on Psychomotor Functions

Psychomotor functions are those aspects of human behavior that necessitate muscular activities as a response to environmental stimuli. Among the various factors that have been identified as fundamental to the performance of such activities are reaction time, dexterity or coordination, speed of activity, and steadiness. Considerable literature exists showing drug-induced decrements in laboratory tests of these skills.

In laboratory tests—generally carried out on normals and usually after single dose administration—reaction time, visuomotor coordination, motor speed, and steadiness often have been shown to be significantly slowed or impaired by antipsychotic drugs (chlorpromazine, perphenazine, thioridazine, haloperidol, chlorprothixene,(5-11)), by antianxiety agents (meprobamate, chloridiazepoxide, diazepam, (12-17)), and by antidepressants (imipramine,(13, 18-20)).

It has been posited that these factors, alone or in various combinations, are integral components in the successful completion of non-laboratory tasks requiring complex motor skills (e.g., operating machinery or motor-propelled vehicles). The demonstration of the above cited drug-induced visuomotor impairments has led to the conclusion that they may constitute serious problems to functioning individuals. In industry, they may result in lowering of production by directly slowing the worker (less pay if on piece-work) and/or by decreasing his precision (more rejected work). They also may jeopardize the safety of the drug-taking worker (and those about him) who is operating machinery. Wherever the operating of a motor-propelled vehicle is involved, the potential hazard also has often been widely proclaimed.

In spite of the fact that many industries possess careful daily (even hourly) production output recordings, injury or accident reports, and health facilities that prescribe and keep records of drugs administered, the writers know only one published article evaluating (on objective performance measures) the influence of psychotropic drugs in an industrial setting. In this study[21], Proctor observed no drug effects that were considered untoward. This void in research clearly needs to be filled.

Numerous articles have been written on psychotropic drugs and driving[22-25]. In each of these studies, the conclusion is clearly drawn that psychotropic drugs produce effects that impair driving performance. The range of warnings goes from the mere admonition, . . . "do not drive . . ." to ". . . no patient on a tranquilizer should drive a car during the course of drug therapy." Indeed, if the results of testing in laboratories, using "simulated driving" equipment, are transferable to on-the-road driving, then these warnings should not be taken lightly. Even the antianxiety agents-meprobamate and chlordiazepoxide—which do not have the profound motor inhibiting effects of the major tranquilizers and antidepressants—have been shown to impair driving ability[6, 26-28]. These studies have shown that not only motoric skills are altered (i.e., reaction time), but also other aspects essential to driving (such as judgment, concentration, and visual acuity) are impaired by drugs.

One would expect a vast body of statistical facts on automobile accidents attesting to the dangers inherent when these warnings are not carried out. (For indeed, many physicians do not stress this danger, nor do they expect their patients to heed their warnings.) However, our search for literature in the area has revealed little in the way of documentation.

A comprehensive report[31] covering all fatal single vehicle accidents over a two year span (1964-1966) was carried out by the State of California. Blood samples were drawn from 772 drivers who died within 15 minutes of the accident, and assays were made for alcohol, caffeine, barbiturates, meprobamate, chlordiazepoxide, and chlorpromazine (phenothiazines) by both spectrophotometric and chromatographic procedures. Of the 772 drivers, only 1% (9 cases) showed any positive reaction for tranquilizers (8 on meprobamate, and 1 on chlordiazepoxide); an amazingly low percentage, when one considers that an estimated 10 to 15% of the adult population is on some form of tranquilizer. Only Murray has published a report[32] which started as a letter in the JAMA, with statistics indicating a tenfold increase in automobile accidents by 68 drivers who had been taking chlordiazepoxide. As substantiating evidence, he subsequently presented the following case report[33]:

> L. K., (54 years old), diagnosed as a chronic depressive disorder with marked anxiety components, was under care and observation for some fifteen months prior to the administration of Librium therapy. His work as a traveling representative had not been impaired following the initial acute phase of his illness although he experienced considerable discomfort. After ninety days on a maintenance dosage of 75 mg of Librium daily, his objective and subjective improvement was indeed dramatic. He reported, however, that he had received a speeding ticket for driving eighty-three miles an hour in a sixty-mile-an-hour zone, for which he paid a fine of $58.00. When he did not receive a receipt from the local Justice of the Peace, the patient informed his Congressman by letter of this default with unusual and unwarranted indignation. A vituperative quarrel with his employer concerning his rate of sales commission soon occurred. (In the past, the patient had related to authority in a passive, acquiescent fashion.) Next, the patient reported another speeding offense within two weeks of the first, and he had had an accident in his brand new automobile backing out of a restaurant car-park into a tree at a precipitous speed because he "just hadn't bothered to look back." This, in a man who had a previously unblemished record of over twenty years driving connected with his work traveling the states of Texas, Oklahoma and Louisiana. Neurological evaluation showed no evidence of incoordination. His response to modified Romberg test was negative. Three weeks later, another collision occurred, this time in a public car-park with a stationary vehicle, and then he reported a quarrel with his local garage over the origin of a mysterious dent in the fender of his automobile, insisting that it had been inflicted by some other individual despite protest to the contrary.

The paucity of reports relating automobile and industrial accidents to drug intake indicates that either patients take extreme heed to their physicians' warnings, or that our fears, based on extrapolation from clinical impressions and laboratory testing, are groundless.

Another possibility may be that neither the patient nor the prescribing physician makes an association between accidents and drug-ingestion. This possibility can explain the absence of reports in the literature.

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BOOK REVIEW

***INSURANCE FOR THE DOCTOR.* By Harvey Sarner, LL.B. and Herbert C. Lassiter, LL.B. W. B. Saunders Co., Philadelphia and London, 1967. 193 pages. $9.00**

Reviewed by: J. F. DUPLINSKY

The authors of this book offer a comprehensive and unbiased evaluation of a variety of insurance coverages that a physician may need in some period of his professional life. It can be used profitably as a reference guide particularly by the young physician just entering practice.

Slightly over twenty percent of the book is devoted to various aspects and programs of life insurance. After some study, a physician should be in the position to develop an insurance plan to meet his needs and income.

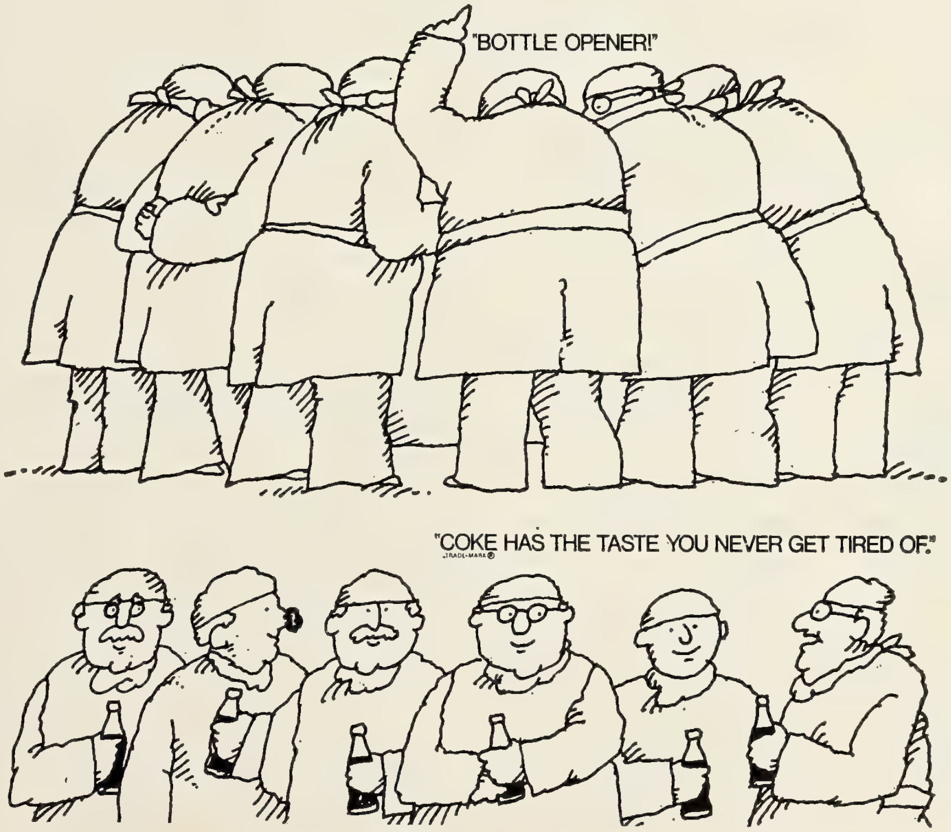
Various approaches to retirement programs are suggested, including group programs offered through national organizations. This phase of planning can be especially important to the self-employed physician. Disability income coverage is explained in some detail, emphasizing the importance of keeping the amount of coverage realistically related to living requirements.

Office overhead expense insurance, health insurance for employees as well as for the physician and his family are also discussed. One of the major concerns of physicians in active practice is malpractice insurance. The authors point out that there may be several exclusions in the basic policy to which the physician should be alerted. These items, such as coverage on the use of X-ray equipment for therapeutic treatment, may be included in an amended policy for an additional premium.

Fire and casualty insurance both for personal and business purposes although important, is less complicated than some of the other considerations under a broad plan of insurance coverage. Automobile insurance is evaluated from the viewpoint of the physician's professional standing and earning capacity in the community. The authors suggest that adequate coverage at a higher level is necessary to protect the physician against the large damage awards being made by the courts today.

There is extensive discussion of a broad insurance program as related to Social Security, unemployment insurance, and Workmen's Compensation. The physician will find one of the brief closing chapters concerning the tax aspects of insurance of particular interest. The authors pose three important questions: Are the premiums deductible? Are the proceeds taxable? How can insurance costs be reduced? An exploration of what constitutes personal or business expense and the dividing line between these two elements including some pertinent examples is covered in this chapter.

For the convenience of the reader, a glossary of insurance terms is provided at the beginning of the book. Certain elements of the various forms of insurance and the choices the physician may make appear somewhat involved. However, this does not detract from the use of the information presented in this book as a guide in conjunction with discussions a physician may have with his attorney, or accountant and, if thoroughly studied, it should place the physician in a more favorable position to discuss his personal insurance needs with his insurance agent.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Report of the 45th Annual Convention

Conducted tours through a unique rehabilitation mobile unit, closed circuit TV programs and an afternoon of continuous health education films were outstanding features of the 45th annual convention of the Woman's Auxiliary to the American Medical Association. The meeting, held at San Francisco's St. Francis Hotel, June 16-19, attracted a registration of 1,741.

Auxiliary president Mrs. Karl R. Ritter, Lima, Ohio, presided over the sessions. The amendments to the bylaws, adopted unanimously, included:

* An increase in national dues from $2.00 to $4.00, which will include a subscription to *MD's Wife.*

* Change to allow the nominating committee to meet somewhere other than in Chicago.

* Revisions in bookeeping and vouchering procedures at such time as may be practical.

Highlighting the four-day session was the mobile demonstration unit called "Homemaking Unlimited." This five-ton coach, sponsored by the University of Nebraska School of Home Economics, shows handicapped housewives how they can be self-reliant homemakers despite physical limitations. The unit contains specially designed homemaking features, such as kitchens, baths, and storage area.

AMA closed circuit TV shows with Auxiliary members as guests attracted wide-spread attention during the convention. The shows, centered around the Auxiliary's supporting role to physicians, allowed its participants to discuss the Auxiliary's community service activities. One five-minute show was aired each morning, Monday through Wednesday. Subjects included "Why an Auxiliary," "The Doctor's Wife Rose," and "Accent on Youth." A fifteen-minute Auxiliary show was broadcast at prime time—6:00 p.m.—Monday through Wednesday. Topics covered were 'Homemaking Unlimited," "Home Centered Health Care," and "Auxiliary Community Service Projects."

The convention formally opened on Monday, June 17, with the keynote address by Philip Lesly, president of The Philip Lesly Co., a Chicago-based public relations firm and PR counsel to the AMA. Lesly urged Auxiliary members to stress the separate responsibility of the physician and strive for improvements that will overcome criticism of the profession. He recommended that they become a vital part of the health care system, by making sure that the key people in it, the doctors, can work most effectively within it, rather than in isolation.

Milford O. Rouse, M.D., 1967-68 AMA President, spoke on "The Physician's Finest Hour" during the Monday luncheon honoring Auxiliary past presidents and AMA officers, trustees and their wives.

The Auxiliary's annual contribution to the AMA Education and Research Foundation amounted to $389,824.64. Eight state Auxiliaries received awards of merit at the Monday luncheon for having the largest percent of increase or per capita in each of four regions. States having the largest percent of increase were: Vermont, Iowa, North Carolina, and Alaska. States having the largest per capita were: West Virginia, Ohio, Tennessee, and Nevada. Seven county Auxiliaries were the recipients of achievement awards: South Central, Idaho; Tuscarawas, Ohio; Macomb, Mich.; Vanderburgh-Southwestern, Ind., Hamilton, Tenn.; Los Angeles, Calif. and Flint Hills, Kan.

The Tuesday afternoon communications program featured Mrs. C. Rodney Stoltz, Communications Committee chairman, Mrs. John Wagner, editor, *MD's Wife,* and Mrs. Paul Sauvageot, contributing editor, *MD's Wife*. Following their discussion, which provided helpful suggestions for communicating as individuals and as a group, films emphasizing the role of motion pictures and health education were shown for the remainder of the afternoon. Mr. Ralph Creer, director of the AMA Medical Motion Pictures Department, gave some valuable pointers on how and when to use motion pictures in Auxiliary programs.

In her inaugural address, Wednesday, June 19, Mrs. C. C. Long, Ozark Ark., suggested focusing Auxiliary programs and an "Accent on Youth." "Not that by any stretch of the imagination do I think that the Auxiliary can solve all the problems of our country," Mrs. Long said, "but I do believe that we can and should do our part for we have a responsibility, as doctors' wives and as citizens, to use what knowledge and what talents we have to help not only the medical profession but this nation of ours."

"We are obligated to help our boys and girls through all the educational means that we have at our disposal," Mrs. Long added. She encouraged Auxiliaries to use wisely available material to implement programs that are needed in their communities.

Other officers installed were: Mrs. John M. Chenault, Decatur, Ala., president-elect; Mrs. G. Prentiss Lee, Portland, Ore., first vice president; regional vice presidents include: Mrs. Lawrence Rapee Bethesda, Md., Eastern; Mrs. Howard G. Ellis, Des Moines, Iowa, North Central; Mrs. Glenn T. Scott, Jr., Ponchatoula, La., Southern; and Mrs. Lyle F. Murphy, Long Beach, Calif., Western; Mrs. Robert F. Beckley, Lock Haven, Pa., treasurer; Mrs. R. C. L. Robertson, Houston, Tex., constitutional secretary; and directors Mrs. Thomas Anton, Maine; Mrs. William Blackstone, Wash.; Mrs. Virgil R. Forester, Okla.; Mrs. Amos N. Johnson, N.C.; Mrs. Clare W. Johnson, Ariz.; and Mrs. Wallace Stacey, Mo.

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Jerome Bobruff, M.D., announces the relocation of his office for the practice of gastroenterology at 425 Montauk Avenue, New London.

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Irving H. Krall, M.D., announces the relocation of his office to 99 Pratt Street, Hartford.

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Marvin L. Prince, M.D., announces the opening of an office for the practice of internal medicine at 5 West Lane, Ridgefield.

Josefina Rodriguez, M.D., announces the opening of an office for general practice at 57 High Street, Stafford Springs.

Joseph P. Shea, M.D., Robert W. Berry, M.D. and S. E. Marrash, M.D., announce their association with Francis W. Mergenthaler, M.D. in the practice of thoracic and cardiovascular surgery at 2660 Main Street, Bridgeport.

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Cooperative Study on Cardiac Catheterization. American Heart Association Monograph Number 20. Edited by Eugene Braunwald, M.D. and Harold J. C. Swan, M.B., Ph.D. American Heart Association, Inc., 44 East 23rd Street, New York, New York, 10010. 113 pp. $5.00.

Current Therapy 1968. Edited by Howard F. Conn, M.D. W. B. Saunders Company, Philadelphia, 1968. 898 pp. $14.00. Canadian price: $15.15.

Medical Physiology, 12th Edition. Volumes I and II. Edited by Vernon B. Mountcastle, M. D. The C. V. Mosby Company, Saint Louis, 1968. Illustrated. $24.00.

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Electrocardiograms of the Month

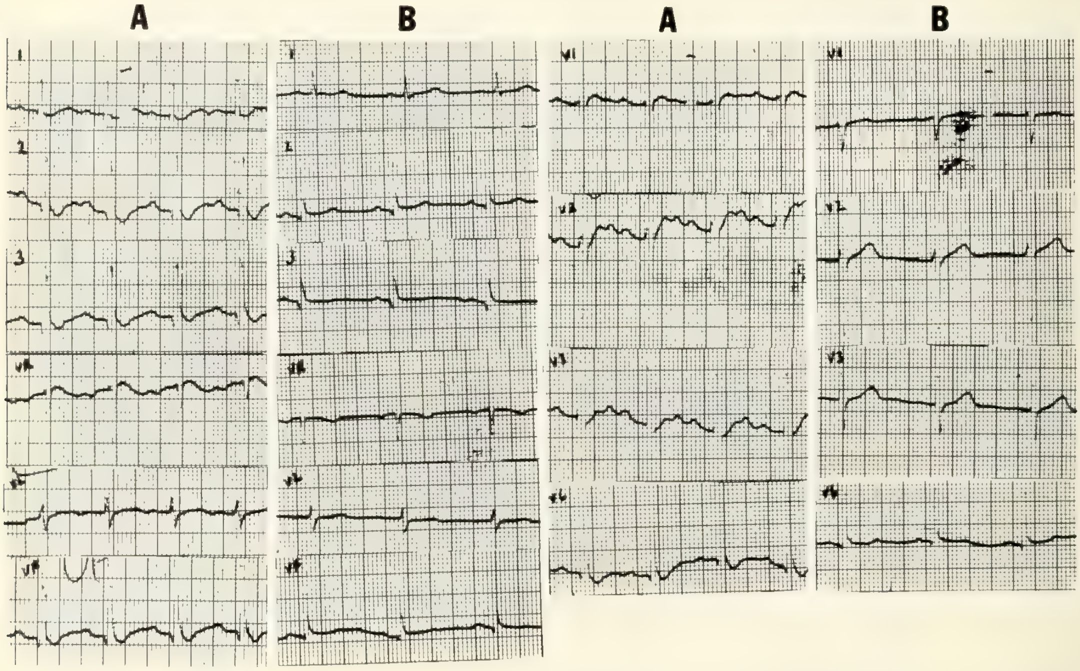
WHAT'S YOUR DIAGNOSIS?

prepared by Hyman M. Chernoff, M.D.,
Director Department of Electrocardiography,
Memorial Unit, Yale-New Haven Hospital,
New Haven, Conn.

A.C., a 53 year old white female, was admitted to Yale-New Haven Hospital on 4-18-68 for repair of an incarcerated femoral hernia. Past history revealed the following: a) thyroidectomy for exophthalmic goitre at age 11. b) recurrent renal calculi at ages 46-47. c) moderate degree of hypertension at age 53, treated with a thiazide drug (Renese). No intake of digitalis or other drugs. d) two year history of severe constipation, recurrent nausea and anorexia, and easy fatiguability.

Tracing A was taken on 4-18-68 as routine preoperative electrocardiogram, before repair of hernia.

Tracing B was taken on 5-4-68, one day after a tumor was removed at a second operation.



Which of the following tumors was found at the second operation?

A—Pheochromocytoma

B—Carcinoid of Appendix

C—Carcinoma of the Gall-Bladder

D—Parathyroid Adenoma

E—Cystadenoma of the Ovary

F—Oat-Cell Carcinoma of the Lung

Tracing A, taken prior to repair of the femoral hernia, reveals the following abnormalities: a) markedly shortened QT interval (K-QT of 0.28 sec.) b) PR interval prolonged to 0.22 sec. c) abnormal T waves in leads 2, 3, VF, and V4. d) Large positive U-waves, especially in leads V2, V3, and V4. In the absence of any intake of digitalis type drug, the finding of a short QT interval and prolongation of the PR interval suggests the presence of hypercalcemia. The prominent U waves suggest the presence of hypokalemia, probably related to the intake of thiazide type diuretic. Because of these electrocardiographic findings, blood chemistry was studied and revealed the following: a) Calcium 17.0 mgm.% b) Phosphate 1.7 mgm.% c) Potassium 2.7 mgm.% d) B.U.N. 20 mgm.% e) normal level of serum proteins. A selenium parathyroid scan failed to reveal any abnormality. At operation on May 3, 1968, a large parathyroid adenoma was removed from the right side of the neck.

Tracing B, taken one day after removal of the parathyroid adenoma, reveals normal values for the PR interval, QT interval, normal U- waves, and normal T waves. Post-operation blood chemistry revealed a calcium level of 9.5 mgm.%, a phosphate level of 3.0 mgm.%, and a potassium level of 4.0 mgm.%.

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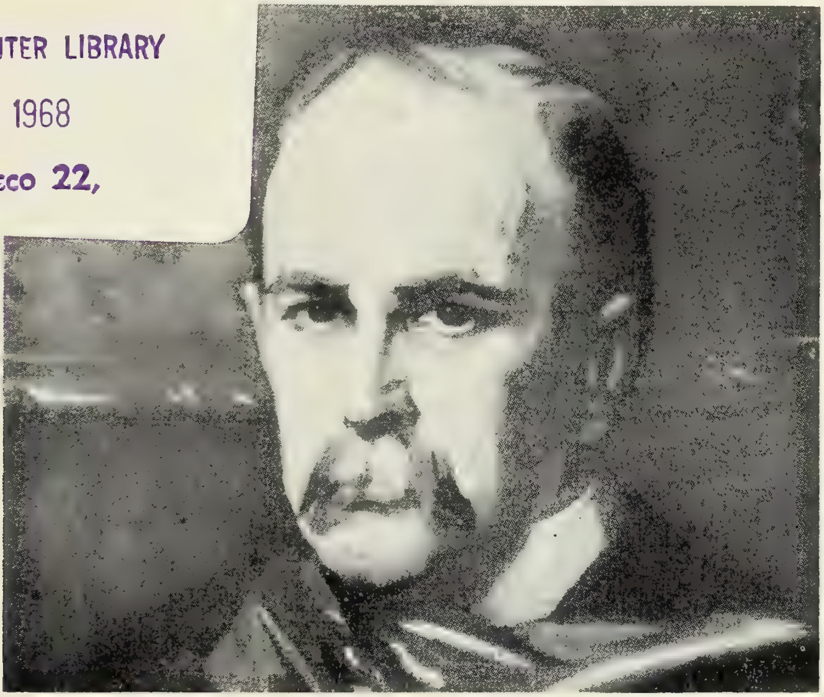

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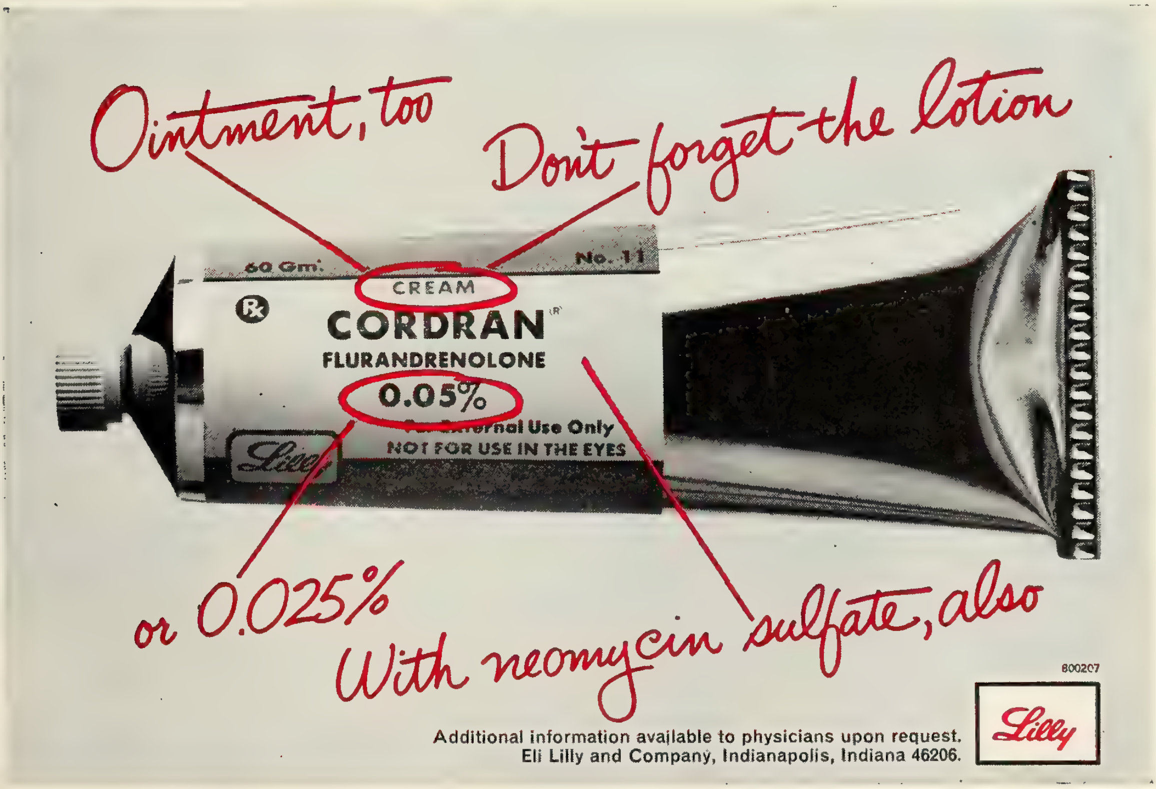

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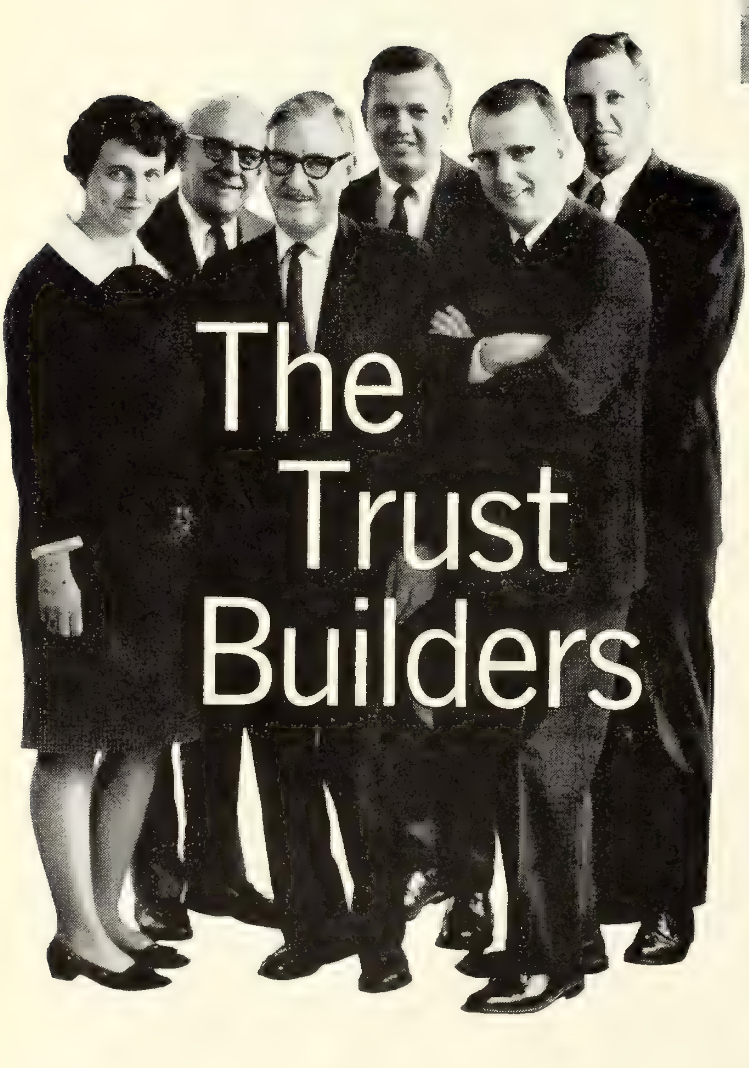

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Connecticut Medicine

editorials

General Practice

Only casual observation of the pattern of medical practice as it exists today would alert one to the fact that the practice of medicine is changing. There are relatively more physicians engaged in limited specialty practice and fewer in general practice which maintains a more personal relationship with the patient and his family. There are fewer physicians trained in general practice now graduating. But more Internists, Pediatricians, General Surgeons and some Psychiatrists join the General Practitioners to help with primary patient care, and closely associated with this group are Sociologists, Psychologists, Podiatrists, laboratory and ancillary medical service people.

Recently various official government agencies and commissions, such as the National Commission on Community Health Services, Citizens Commission on Graduate Medical Education and the Ad Hoc Committee on Preparation for Family Practice, all three of these groups—the Folsom, the Millis and the Willard Commissions which reported in 1966—have taken a positive stand for the need for specially trained physicians to render family health care. The American Medical Association, as well as its respective state medical societies and the American Academy of General Practice have long adopted a positive program to encourage General Practice. Some medical educators have added their views to support the recommendations of the aforementioned commissions and agencies.

One approach to the problem is to stimulate newly graduated medical students to take training in General Practice and such a program will be helped by 1. the creation of the proposed board specializing in family practice, 2. official assurance of hospital status, 3. membership in a group to assure complete high quality medical care for the patient, and 4. permanent staffing of the hospital emergency room to allow the physician relief time for courses, vacations and a more balanced family life.

Some medical groups have proposed different solutions to this problem such as the use of Internists as General Practitioners, combined Internists and Pediatricians as the family care unit, and recently a four-year post graduate training program for the physician to become a combined Pediatrician and Internist to serve as the primary family physician. Other groups, such as the one at Duke University, have suggested using two-year college trainees as medical clerks to make house calls and refer patients to an appropriate physician. Other suggestions included using R.N.'s to be the patient's first contact and recommend proper treatment. This inevitably must lead to confusion in the present-day medical practice and this confusion can be resolved when there is a thorough understanding by all concerned of what the patient's needs really are and how they can best be served under present-day conditions.

In order to play the most meaningful role, the family physician is improving his own work through a variety of endeavors: taking post graduate medical courses annually and thus maintaining his flexibility in an ever-changing world by being a perpetual student; broadening his skills by taking psychiatric training; participating in self-evaluation courses; assisting his hospital in all available departments by doing his share of emergency work and offering his help in hospital clinics and community health programs.

The General Practitioner has now become a well-trained physician who has graduated from a Class A approved medical school, completed an internship or a two- or three-year internship and residency program in an approved hospital and has proven himself to be competent in his own community, his hospital and with his associates and his peers. The personality of this physician is usually patient-oriented throughout his medical school and post graduate training. His function in his community has become that of correlating the necessary specialized care for the patient after he has diagnosed and treated the presenting problem. He serves as a guide for psychiatric, sociologic and public health aspects of health problems. His ability to give continuous care to the family in all age groups and within the framework of the home and the community gives stability to the doctor-patient relationship.

The nature of his work is such that should permit his continuous association with hospital-based specialists and medical educators who, it is hoped, would allow him to take part in lecture programs presented to medical students and encourage his participation in clinics and ward rounds in an atmosphere of respect and mutual assistance, in turn helping him to retain a vigorous interest in his practice, making his fellow physicians respect him, his peers proud of him, and his patients devoted to that altruistic principle for which he stands.

The establishment of the proposed boards in General Practice is indeed an encouraging trend. What is of equal, if not more, importance to the experienced physician, however, is formal recognition and certification by the appropriate academic and A.M.A. committees of the overall quality of his medical performance in terms of his daily practice, the improvement of his skills, and his keeping abreast of the latest advances in medical science. Formal certification for this type of physician would carry more prestige, placing him above the limited specialties and establishing him as the key member of the medical team.

At a time when Government is beginning to play an important role in the private sector of medicine, all physicians in all categories should realize that they must be concerned with society's interests in the health care field. The medical profession must now realize that it should evolve a new philosophy and this will require active participation not merely in medical societies but also on hospital boards of directors, community health programs and government health programs.

Waldo E. Martin, M.D.,
Guest Editor

Education For Family Practice

To improve the teaching of students and to recruit them into careers as family physicians a unique Department of Family and Community Medicine has been organized as an integral part of the new four year College of Medicine of the Pennsylvania State University of the Milton S. Hershey Medical Center in Hershey. The departmen is on the same level as traditional clinical departments. It will consider many questions relating to family medicine. Is family medicine a discrete body of knowledge which clearly can be accepted by the Public and the profession? The medical problems now cared for by the physicians in family practice require some knowledge of most of the clinical disciplines as they are practiced by specialists.

Is family practice a pattern of delivery of medical care? Does the public want a single physician of its choice not only to look at the disease in the individual member but at the unit of society, the family living in a specific community? The decision will rest with the public. We all see around us how more and more patients are selecting their physician on the basis of self diagnosis and self referral.

Is family practice an attitude of mind in the physician? The family physician has the professional responsibility for making medical decisions involving all members of the family. We believe this attitude of mind on the part of the physician should be developed regardless of how he ultimately may limit his practice.

It is expected that at Hershey the members of the new department will serve as role models for students throughout the four years of the curriculum. They will demonstrate to students through their practices the application of social, behavioral, cultural factors in programs of medical care. The present members of the department appointed are three physicians now practicing in Hershey who have records on their patients extending over a period of ten years or more. This requirement appared necessary to assure the student recognition of the need for continuity of care. In this fashion the University has assumed direct responsibility for medical care for the segment of the community represented by the practices of this department. The full resources of the University Medical Center will be available to these physicians for application to patient care.

The physicians will move their offices into the medical science building. But the patients will be seen in an office setting most nearly resembling in character that of their present offices in a residential area. The offices will not resemble the usual out-patient clinic. However, the student will be able to compare the two settings, private doctors offices and the traditional out-patient clinic setting. They plan to have the initial patient contact of the student in the very first month of his first year with ambulatory patients of the family physician.

The members of the new department will be full-time faculty and will be eligible for tenure in the University on exactly the same basis as any other faculty member. They will have the same privileges and responsibilities as the specialists and their income limitations similar to other full-time faculty members. Their patients will be admitted to the regular wards of the teaching hospital. The teaching will be largely informal involving a single or small group of students not exceeding four. The students will also have weekly individual sessions in the office of a member of the new department. The student will also follow the family with the physician into the home and ultimately when necessary into the hospital.

Interaction within the family to external stresses or to illness in a member can then be demonstrated and the importance of continuity in care over a period of years will be emphasized. As particular acute problems arise requiring specialized care, the use of consultants for help can be demonstrated. The use of the laboratory and need of diagnostic procedures of varying degrees of sophistication can be kept in perspective. The actual use of the laboratory in comparison to former years in the same physicians practice will become clear. The value of periodic multiphasic screening from the laboratory point of view in the early detection or prevention of incipient disease in a cross section of the society will be clarified. The application of genetic and other basic biological principles to premarital counselling and family planning for children can be easily taught in this fashion. Finally the application of behavioral disciplines to solution of marital problems, behavioral disturbances in children, the stresses of adolescence with its ups and downs of mood can be demonstrated.

Obviously the members of the new department will have to prepare themselves by spending the equivalent of one year in post-doctoral training. They will take periods of two to four months each year in residence in a major medical center, serving in depth in medicine and pediatrics where general problems are seen. They will work in clinics, in seminars concerned with marital problems and the care of the adolescent. They have already done such work in Boston, Washington and Philadelphia. It is anticipated that each faculty member will spend one period abroad observing patterns of social and community medicine in other countries. The department members have found this pilot experiment for a different pattern of continuing education both stimulating and valuable. The setting in a teaching hospital was chosen as the one in which the physician experienced the maximum period of learning during his training especially in the techniques of clinical problem-solving and the development of clinical judgment.

Certain results have emerged from this pilot experiment that augurs well for the future of the trained family physician. The pilot experience, though it required considerable adjustment on the part of members of the new faculty indicates an unexpected beneficial effect on the teaching of the

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house staff from the view of the practicing physician. The individuals have demonstrated quite superior qualifications aside from practicing physicians in becoming leaders in many community projects and students are quick to recognize these other qualities. The department is expected to serve as the educational focal point for the application of material taught by the department of humanities and behavioral sciences.

The department now opens opportunities for research inpatient care. Studies can now be carried out on the change in use of the laboratory and in the use of paramedical personnel to render comprehensive continuing care. The possibility certainly exists for development of a new type of aide to the physician who might be called a family health advisor or social worker to work out of the private physician's office in the home for continuing instruction of the family unit in the meaning of an illness and the details of home care. It would be possible to add to the department additionally scientifically trained personnel in the fields of epidemiology and genetics to give a firmer base for teaching clinical research and patient care.

The emphasis in teaching will be on the individual relationship between the student and instructor, patient and physician and every effort we are promised will be made to avoid institutionalization of patient care. Even though the physical setting is in an institution and its facilities back up the individual the philosophic orientation will be different. For in addition to their offices, the members of the department will have available an ambulent unit for minimal or self-care of patients who do not require full nursing service. The unit is decorated to capture the feeling of a home and to permit a member of the family to stay with the patient during diagnostic studies or convalescence from an acute illness. They will, of course, require also a separate extended care facility in the form of a nursing home.

This experiment in education of the physician in delivery of medical care to the family is expected to improve the recognition by medical students of the impact of disease biologically, culturally and socially in the setting of a family living in a community. The commitment of students to careers as famiy physicians will be fostered. Additionally is the development of attitudes of the family physician to each student regardless of the type of practice he may ultimately enter.

L.H.N.

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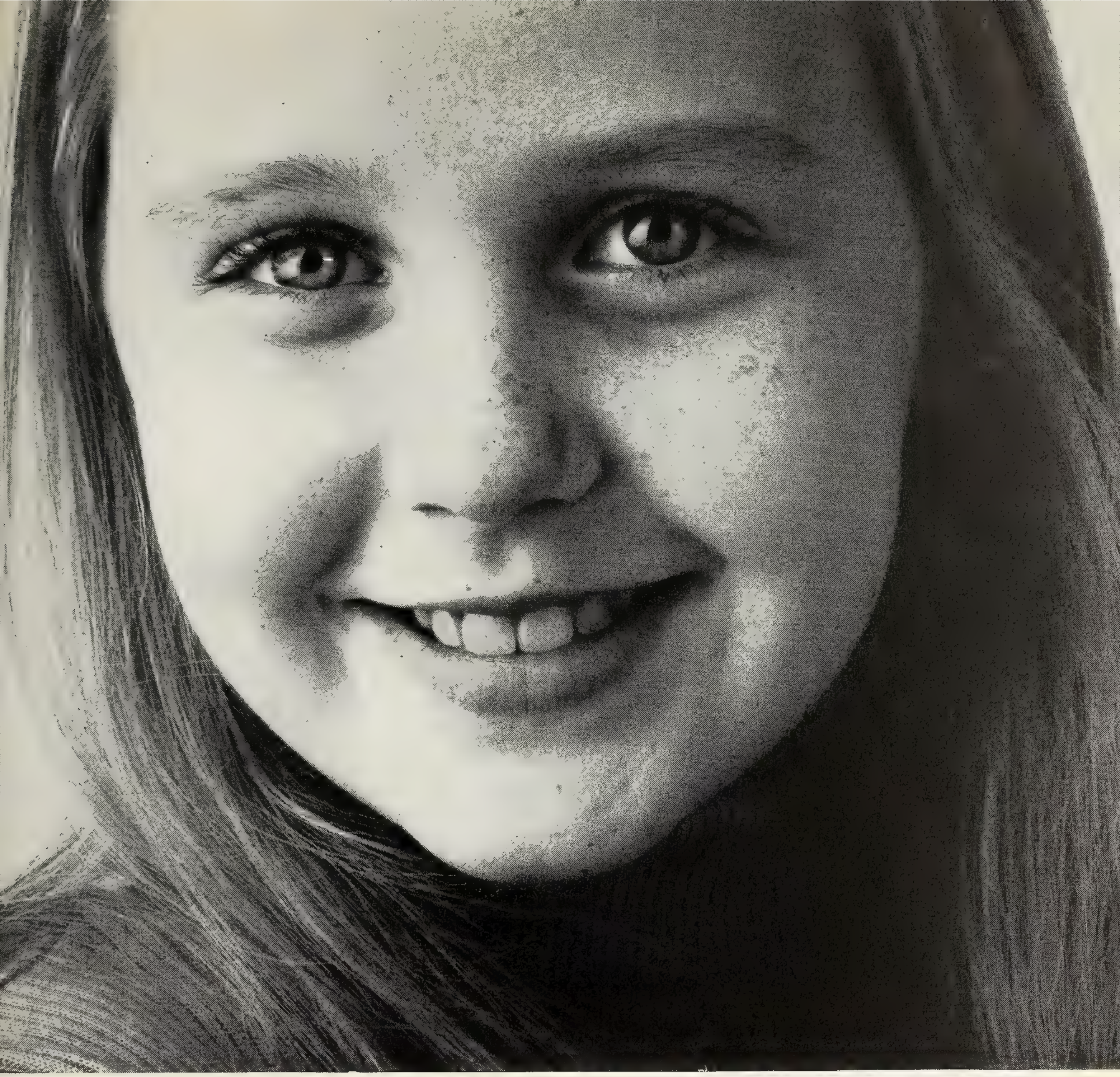
Basic Science And Practical Medicine: Gout

It is the role of the basic medical scientist to try to provide a foundation for the understanding of the normal form and function of the human animal, the better to understand the deviations from the normal which is disease. With such an understanding the physician can proceed rationally to diagnose and to treat. Without such an understanding, diagnosis and therapy may be effective but must by definition be purely empirical. Gout can be considered an example of how basic science has illuminated and led to the true conquest of an age old disease.

Since Hippocrates time it has been known that this is an affliction seen predominantly in the male, familial in distribution and characterized by bouts of very painful acute articular inflammation, the gradual growth of tophaceous masses in the cartilage of the body. That colchicine specifically interrupts the acute attack has been recognized intermittently since the work of Alexander of Tralles in the sixth century A.D. In the absence of any basic information, these and other facts about gout could be tabulated, memorized and recognized but certainly not understood. Even today there is a great deal about gout that is quite mysterious. Still progress has been made. One is the recognition by Wollaston that tophi were largely composed of crystals of sodium urate. Another is the subsequent observation that gout is generally accompanied by an elevation in the level of serum urate concentration. Another is that urate deposit in the kidney leads gradually to its destruction and that in such patients urate crystalluria is not uncommon.

In other animals there is present an enzyme uricase which oxidizes urate to a more soluble allantoin before renal clearance. This enzyme is missing in man. Since the entire species does not suffer from gout, the absence of uricase alone is not a sufficient condition for gout. Many studies over the past twenty years have revealed a multiplicity of mechanisms that may lead to gout. Some "secondary" such as failure to adequately secrete urate in chronic renal disease. More interesting is the overproduction of uric acid which may be readily demonstrated in many victims of gout, even when they are placed on a purine free diet.



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With the advent of isotopic tracer methodology it became relatively simple to measure the rate at which isotope was incorporated into uric acid when administered in the form of one of the known purine precursors such as glycine labelled with ^{15}N and subsequently with ^{14}C. From measurements of the isotope excreted in urinary uric acid it has become possible to estimate with reasonable precision the rate of purine biosynthesis. This methodology by a most fortunate circumstance was employed by Lesch and Nyham[1] in 1964 in an unusual case of a child in Johns Hopkins Hospital who presented with hematuria as a result of urinary tract calculi which in turn proved to be uric acid stones. A moderate degree of hyperuricemia surely not common in children was further explored and was found to be an exorbitant over production of uric acid as measured by isotopic glycine incorporation.

This relatively rare defect is now known to be due to an inborn metabolic error observed in male children and is apparently transmitted as a recessive gene borne on the X chromosome. The complete syndrome is characterized by mental retardation, choreo-athetosis, grossly abnormal aggressive behavior with episodes of self-mutilation, and marked hyperuricemia due to enormously exaggerated overproduction of urate. This in turn leads to uric acid crystalluria, calculi and occasional clinical gout. The enzyme defect that accompanies and is presumably responsible for the clinical signs and symptoms has now been identified by Seegmiller et al[2] as total lack of phosphoribosyltransferase. Because of the absence of this enzyme there is a deficiency of nucleotides which normally holds uric acid synthesis in check. Here at least is one species of gout for which the pathogenesis is a fairly complete story.

The curious and diagnostically specific response of acute gouty arthritis to colchicine is also beginning to fall into line. In Seegmiller's laboratory,[3] it has been shown that sodium urate dispersed in microcrystalline form is avidly phagocytosed and such phagocytosis can be demonstrated in the joint fluid of the gouty patient. The non-gouty subject usually maintains a level of urate in body fluids such that crystallization does not occur. In prolonged hyperuricemia crystals may be found not only in the cartilage (tophi) but also in joint fluid. Phagocytosis results in marked increase in glycolysis by the leucocytes with generation of lactic acid and in the closed joint space a decline in pH. in the joint fluid. This in turn further reduces the solubility of urate leading to further crystallization. Colchicine interrupts this cycle dramatically, decreasing phagocytosis. Colchicine destroys the appetite of the leucocyte for microcrystals. In this way colchicine tends to relieve the inflammation of the joint but does not affect the hyperuricemia.

Thus a rational approach to the curious disease is beginning to appear, steps that must be directed against high uric acid levels in the serum. Uricosuric agents such as probenecid have proved their usefulness especially in tophaceous gout, since prolonged administration does in some cases lead to disappearance of tophi. This regime, however, suffers from one defect. It loads the urinary tract with a great deal of poorly soluble urate, a situation favorable to calculi formation. Very great interest therefore attaches to reports over the past few years to allopurinol that specifically inhibits the enzyme xanthine oxidase[4] and thus prevents formation of uric acid.

This new pharmacologic approach has provided a product that lowers the level of serum urate not by increasing renal clearance, but by blocking uric acid synthesis. The patient whose urinary purine before treatment was almost solely uric acid, now under treatment divides his purine load among hypozanthine, zanthine and uric acid depending upon the degree of xanthine oxidase inhibition achieved. Thus the level of serum uric acid will decline, without imposition upon the urinary tract of the burden to dispose excessive uric acid. The likelihood of calculus formation is reduced, of microcrystalline formation in joints and of urate deposit in the kidney also.

This story exhibits the complimentary nature of the basic and clinical sciences.[5] Without a biochemical physiologic or pharmacologic base, the clinician can only imperfectly understand what he is doing. In turn, however, the biochemist needs such clinical entities as gout or the Lesch-Nyhan syndrome to draw upon and without which his work would be greatly impeded. The clinic provides to the basic scientist not only important motivation but also an array of genetic defects often expressed as single enzyme deletions that are not otherwise obtainable.

The continued integrated application of basic and clinical research skills supplemented by an occasional "happy accident" such as the unearthing of a particularly informative mutation will surely serve to shift that which is chiefly emperical toward that which is rational. Gout is an excellent example of this concept.

L.H.N.

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Keeping Drivers Alive And Driving By Decreasing Injury On The Highway

We have seen that the largest percentage of fatalities occur in the younger age group with young males predominating. Furthermore, driving training is important although the techniques of measuring the effectiveness of training still needs to be improved. Drivers may be influenced by personal and emotional maladjustments and the role of excessive drinking is very important. Much still remains to be done for an understanding of the role of disease and illness in auto accidents and more reliable criteria for disqualification are urgently needed for licensing authorities. Then there is the design of highways which leaves much to be desired in eliminating accidents resulting from human errors and in this regard the influences of poor lighting appears to be of great importance.

Apparently it is not safer to be thrown clear in an accident. It is much better to remain inside the car.[1] Seat belts will rarely produce injuries even in severe crashes. Nor will they often entrap the occupant inside even if a car falls into deep water or catches fire. The new American autos are now equipped with shoulder belts as well as seat belts. Unfortunately many drivers and passengers will not use this new life saving equipment, just as thousands never used the seat belt alone. But the general public would probably use the combination of safety belts if they really were convinced that it increases the chance of survival and of sustaining fewer and less severe injuries in auto crashes.

Across the chest harnesses have been the source of some controversies because convincing evidence of this added efficiency compared with ordinary lap belts has been lacking. Now, however, a remarkable

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study in Sweden seems to offer proof that the three point harness does prevent injury and does save lives. Bohlin[2] furnishes statistics for a large number of accidents involving two models of automobiles. The manufacturer has recently installed combination seat belts in all cars built since 1959. Since the manufacturer guarantees every car for post-accident repair costs in excess of eighty dollars, all serious accidents probably will be known to the company. On this basis Bohlin believed that the data are unusually complete for analysis.

In order to collect on this guarantee each auto owner whose car is damaged is asked to complete a questionnaire designed to accommodate a computer program. Through the company, Bohlin received data from 28,780 accidents involving 43,813 occupants. In 1,803 of those accidents 2,445 occupants received injuries varying from slight to fatal. Although over 98 per cent of the counties involved had seat belts installed, the belts were worn at the time of the accident by only about 25 per cent of drivers and 30 per cent of the other front seat occupants.

On the basis of these figures one would expect injuries to be distributed in a ratio of 3:1 for unbelted occupants compared to those wearing the belts if the belts played no role in preventing injuries. Yet in this series there were 49 unbelted front seat occupants killed but only three occupants who wore the seat belts, not the predicted 16–17. The figures are particularly striking when related to auto speed at the time of the accidents. All three fatalities of belted front seat occupants occurred after accidents at speeds exceeding 60 m.p.h. But death among those not wearing seat belts occurred over the whole speed scale, one at a speed as low as 12 m.p.h.' Bohlin reports that in his series many subjects wore their harnesses too loose when it should be snug. Nevertheless only 59 per cent reported injuries caused by the seat belts themselves and most of the injuries were trivial and minor.

There seems little doubt that a combined lap and diagonal shoulder harness worn properly will reduce the frequency of injury and death in auto accidents. But simply knowing this will not by itself save lives or prevent injury unless drivers also use the restraining devices. Clearly consumer reluctance to use this combination harness must be overcome. Convincing the public is a task at which auto manufacturers and the insurance industry can excel. Their own self interest should dictate that it is preferable to keep drivers alive and driving.

McFarland's studies of windshield injuries has led to doubling the plastic layer and the bonding loosely attached to the glass. This new improved penetration resistant glass introduced in 1966 is significantly reducing facial lacerations without increasing intracranial and neck injuries. At present with the use of seat belts there is a tendency for the upper part of the body to lurch forward on impact at the time of the accident. The seat belt gives some protection for the knees, but the head and thorax as it flexes forward will strike the intrument panel and hit the steering wheel or the windshield. Commonly the mandible is spared because the middle third of the face strikes the instrument panel. This forward lurch of the head is restrained by a shoulder harness properly applied.

As a result of what we already know about traffic accidents and how to avoid them some positive aspects of automotive safety have emerged. The first, of course, is that drivers should be thoroughly acquainted with the rules of the road. The second is to have a tune-up for the family car in May since it will be used increasingly during the summer. Third, is the seat belt campaign as it concerns their proper use. It would help to have radio and television announcement reviewing one or more rules of driving on the nation's expressways. Fourth during holiday weekends drivers could be urged to take frequent rest periods with emphasis on some sort of nourishment. Who knows how many accidents have been caused by irritability and impatience brought on by fatigue and low blood sugar.

Much travel is out of state and drivers should be made acquainted with traffic and safety laws in another state. Another is to recommend the driver to see his doctor for a spring check-up with a "tune-up" if necessary. It is hardly logical to have a mechanically perfect automobile if the operator has become impaired in the meantime with sickness, reduced vision or by drugs. Major impairment will undoubtedly be known to the driver but change in eye-sight and hearing can occur subtly and imperceptibly over a period of time.

L.H.N.

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Research Related To Dentistry: I.

Oral pathoses exemplify particularly well the principle that infectious disease develops not merely due to the presence of a germ, there must also be contributing environmental factors as well. This concept, optimum conjunction between germ and environment is well exemplified in the problem of dental caries, a disease in which bacteria produce acid decalcification of dental hard tissues. What then in the presence of the appropriate bacteria is responsible for host susceptibility and resistance?

Many bacteria are cariogenic but attention is now directed to a group of anerobic streptococci found in the human and animal oral cavity which form both extracellular and intracellular polysaccharides. The extracellular polysaccharides are responsible for their adherence to the tooth surface as dental placques. The intracellular polysaccharide accumulates during the period of intake of dietary sugars by the host and is fermented to lactic acid which prolongs the period when acid decalcification can occur. An important factor also seems to be variation in the ability of the microorganisms to implant themselves in the particular host on a particular diet. Some streptococci have little ability to synthesize extracellular polysaccharides from sucrose and are consequently unable to adhere to smooth surfaces of teeth unless they are trapped mechanically in pits and fissures of teeth, then they initiate caries. These findings have been derived from a study of germ free rats infected with bacteria from human placques.

An important environmental factor influencing the caries forming process is the presence or absence of fluoride in the apatite crystals of enamel. How fluoride renders the crystalline structure of enamel less susceptible to attack has received much study. The lattice perfection of enamel improves with increase in fluoride content. This renders it a more perfect structure so that the enamel is now less soluble in acid. One question remaining is whether a higher fluorine content in the surface layer affords any real protection in permanent teeth. This knowledge would resolve the question whether it is fluoride intake or fluoride application that is protective. Fluoride also seems to play an important role in the process whereby collagen in bone and teeth becomes calcified. Apparently fluoride inhibits elastin mineralization and by slowing this process causes more slowly forming stable mineral bone.

There has also been much research on connective tissue especially as it relates to periodontal disease (pyorrhea). In this disease there is progressive destruction of the periodontal ligament and alveolar bone surrounding the roots of the teeth. In studies of the formation and destruction of connective tissue a recent clue now implicates the enzyme collagenase in the destructive process. High degrees of endogenous collagenase activity have been found in gingival tissue under normal conditions and strikingly increased concentrations have been found in biopsy samples from patients with periodontal disease. The collagenase detected appears to be that involved in the normal metabolic turnover of collagen. Work is progressing on the further purification of this enzyme derived in quantity from cultures of human gingiva and more recently from human granular leucocytes.

Concurrent studies have revealed a low but significant level of collagenase in normal skin with striking elevations associated with certain systemic disorders such as amyotrophic lateral sclerosis. Recently collagenase and hyaluronidase activity have also been demonstrated in diseased human gingival tissues and in synovia from patients with rheumatoid arthritis. Then there is research focussing on the structure of the collagen molecule. Insoluble collagen is of unique interest since it comprises the predominant organic substrate of bone and dentin. Standard techniques have been applied to determine amino-acid sequences in peptides derived from cleavage of collagen. Apparently different collagens have different properties and functions in different tissues of the same animal.

Much investigation is also going on in causes of the cleft palate. In this country one of every 750 children is born with a cleft palate. Research thus far has focused primarily upon rehabilitation of these children by means of better surgical and dental management, improved speech therapy and other measures. Now efforts are being directed to better understand the causes of clefting as a step toward its prevention. One approach is through experimental teratology with a drug chlorcyclizine and methods of preventing its teratogenic effect. Studies also have implicated derangement of vitamin D_2 metabolism during pregnancy leading to cardiac, facial and dental anomalies especially malocclusion, dental cross-bite and hypoplastic incisor teeth.[1]

L.H.N.

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Another Risk Factor In Coronary Heart Disease: Defective Fibrinolysis

During the past ten years evidence has been growing that some patients with occlusive vascular disease differ from healthy people in the fibrinolytic activity of their blood. Men with arteriosclerosis of the lower limbs have a higher evidence of defective fibrinolysis than do controls. However, the results in patients with coronary heart disease (CHD) have been discordant probably because of failure to consider the influence of age as Chakrabarti has pointed out.[1] In an initial investigation by the dilute blood clot-lysis time in survivors of myocardial infarction and age-matched healthy people, these workers found that 45 per cent of the patients below age 60 had defective fibrinolysis as judged by a lysis time of seven hours or longer, compared with 8 per cent of those older than 60 and 10 per cent of controls.

These results depended on a single estimation and now the work has been repeated using three estimations of the dilute blood clotlysis time in 107 male survivors of myocardial infarction and 90 age-matched healthy controls with normal electrocardiograms. The results bear out the previous findings and indicate that defective fibrinolysis should no longer be ignored in relation to the genesis and prognosis of myocardial infarction. Below the age 50 half of the patients with CHD compared with one-fifth of their controls had low fibrinolytic activity. Between age 50-59, one-third showed diminished fibrinolytic activity as compared to 10 per cent of controls. As noted after age 60 the incidence of reduced fibrinolytic activity had dropped to 10 per cent.

One might theorize as Chakrabarti does that the patients with early defective fibrinolytic activity had died by the age 60 and that a defective fibrinolytic system has a sinister effect on prognosis. The fact that only 50 per cent of patients with myocardial infarction showed defective fibrinolysis indicates that half of all such patients develop coronary occlusion through a mechanism other than thrombosis, probably that due to subintimal hemorrhage. Nevertheless, if half of the patients with myocardial infarction have an abnormal fibrinolytic mechanism, it suggests that this may be of pathogenetic significance in an appreciable number of patients with coronary occlusion. We must, therefore, add this "risk" factor to the others already established such as smoking, obesity, hypertension, hypercholesterolemia and hyperuricemia.

On the assumption that natural fibrinolysis is an important protective mechanism against vascular occlusion it would follow that pharmacologic fibrinolysis might be a useful prophylactic measure in those survivors of vascular accidents who have a defective fibrinolytic mechanism including those who sustain a myocardial infarction. Such patients could be readily identified by determining the dilute blood clot-lysis time.

Over the past ten years Chakrabarti and his group have been attempting to find a pharmacologic means of enhancing fibrinolysis. They tested a variety of drugs that would do this when given by mouth. Most of them led to the development of resistance to the fibrinolytic effect which developed after 3-12 weeks of treatment. The problem of resistance has now been overcome by combining two oral fibrinolytic drugs, phenformin (given in a sustained release capsule) and an anabolic steroid ethylestrenol. This combination of drugs seems to be non-toxic, is well tolerated by most patients and produces a sustained increase of blood fibrinolytic activity of the order of 50 per cent.

In nearly all patients with defective fibrinolysis, phenformin plus ethylestrenol will increase fibrinolytic activity to normal levels for as long as the drugs are given, up to three years according to present experience. In addition this combination of drugs reduces plasma fibrinogen levels by about 25 per cent and serum cholesterol levels by about 15 per cent. The two drugs were also found to have reduced platelet stickiness by about 50 per cent in 15 of 20 arteriopathic patients to whom they were given.

The findings reported by Chakrabarti, et al support the trial of phenformin plus ethylestrenol as a long term prophylactic measure in those survivors of myocardial infarction who have deficient fibrinolysis as measured by the dilute blood clot-lysis time. If platelet adhesiveness is a factor in arterial thrombosis[2] then reducing this factor might also prevent arterial thrombosis, in which case it may turn out that pharmacologic fibrinolysis could be protective against a second coronary occlusion in all post occlusive patients.

L.H.N.

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The Effect Of Cigarette Smoking Upon Small Arteries And Arterioles

When cigarette smoke is inhaled, all structures in the pulmonary parenchyma including arterioles and small arteries are brought into close proximity to toxic products in cigarette smoke. Auerback, et al[1] have shown that the walls of blood vessels in the pulmonary parenchyma of cigarette smokers show definite thickening. Clearly the vessels develop pathologic changes as a result of the influence of the toxic products[2] present in cigarette smoke. The question arises however whether the vascular thickening in the pulmonary parenchyma is only a localized phenomenon in cigarette smokers or whether there develop systemic effects as well. This is an especially important question since many of the toxic products inhaled by cigarette smokers enter the blood stream as well as producing local irritative effects.

Auerback, Hammond and Garfinkel[3] have addressed themselves to this problem and have measured the degrees of fibrous thickening in the walls of arteries of several other organs of smokers and have analyzed their results in terms of age and degree of cigarette smoke inhalation. In addition to the trachea and bronchial tree they studied the arteries and arterioles in the esophagus, the stomach wall, the pancreas and the adrenal glands, for if the vascular damage in smokers is more widespread than that in the trachea and bronchi, then it would help to explain the much higher incidence of coronary heart disease found in cigarette smokers.

In five independent studies the authors found vascular changes in all these organs studied. They took one specimen each from 925-1025 subjects taken at autopsy from the adrenal gland, stomach wall, esophagus, pancreas. There were a total 8764 sections. The microscopical findings were analyzed according to smoking habits and by age. They found that in all five locations the degree of fibrous thickening tended to increase with age, tended to be considerably greater in cigarette smokers than in non smokers and tended to increase with the amount of cigarettes smoked.

The findings in this study amply confirm the presence of damage to vessel walls in the bronchopulmonary tree where the vessels are directly exposed to cigarette smoke. Obviously another mechanism must be responsible for the association found between cigarette smoking and fibrous thickening of walls of arterioles and small arteries located in tissues that are not directly exposed to the toxic products in cigarette smoke. The mechanism though not decided upon as yet, must certainly be due to the effects of the toxic products absorbed by blood and carried to the affected arteries.

Regardless of the actual mechanism, it is difficult to believe that thickening of the walls of arterioles and small arteries located in an organ could not but have a deleterious effect upon that organ. If widespread as now seems to be established in this study, it may place some strain on the cardiovascular system as a whole. Is this the factor bearing on the increase in death rates from a multiplicity of diseases with advancing age and with the amount of cigarette smoking?

L.H.N.

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Sleep Treatment In Acute Myocardial Infarction

The risk of death from acute myocardial infarction appears to be greatest at the onset of the illness. When deaths occur among such patients reaching the hospital some are accounted for by development of a fatal arrhythmia. In fact the prevention of these electrical catastrophes is a major objective of the coronary care units, because some are not the result of irreversible heart damage. While it is important to realize that the incidence of major arrhythmias increase with the severity of the infarction as judged by presence of hypotension, shock, congestive heart failure and ectopic beating especially below the a-v node, the fact is that certain procedures can be done to minimize the arrhythmias, such as use of oxygen mask, administering anti-arrhythmic drugs such as lidocaine and atropine in a-v block and isuprel in idio-ventricular rhythms.

It is now recognized that pain and mental distress may be important etiological factors in death from arrhythmias. In the cardiac catheterization laboratory and cardiac surgery recovery room care is taken to avoid pain and fear. Anesthetists have known the risk of sudden death in frightened pa-

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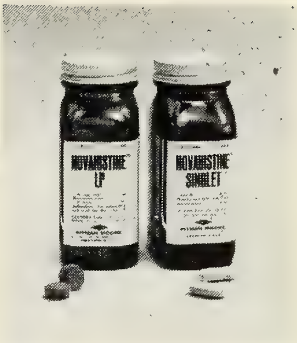

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tients since the time of Lauder Brunton. Pain and fear cause an over active sympathetic discharge to the conduction system and muscle fibers in the heart and increases ectopic activity and the threat of ventricular fibrillation after coronary occlusion in animals. Wallace, et al[1] have drawn attention to the relationship between psychologically stressful events, increased catecholamine excretion and arrhythmias in cardiac infarction in man.

Why not then use a regimen designed to reduce pain and mental distress by producing a state of contented light sleep during the period of greatest risk from arrhythmias? Nixon[2] tried this on fifty-nine patients admitted less than twenty-four hours after onset of symptoms of acute myocardial infarction. Patients were put to sleep with promethazine and pethidine (demerol) administered intravenously as soon as possible. Expert nursing care was constant. Three times daily the patient was allowed to awaken for oral fluids. The majority were disinclined to eat, and for doing the breathing and leg exercises prescribed to prevent phlebothrombosis. As the patients were kept asleep, they breathed oxygen by mask and received i.v. dextrose and water, 10,000 units of heparin if not contraindicated was injected six hourly for three days or for as long as the patient was kept asleep.

The authors did not fail to treat hypotension with 5 per cent dextrose infusion and employed digitalis when congestive heart failure was detected. If pain was severe demerol was repeated and if restlessness was severe more promethazine was given and repeated until on arousal patient looked well rested, free from agitation, pain and hypotension, or impaired peripheral circulation or arrhythmias. The duration of sleep treatment ranged from one to seven days and averaged two and one-half. The patients remained in CCU three to five days from the end of the sleep regimen. Other cardiologists have used (elavil) for similar reasons and kept their patients similarly relaxed and half asleep.[3] This might be a better drug to use than promethazine and demerol especially since some patients did not tolerate their sedation well, showing restlessness, nausea and even vomiting.

The results of the sleep treatment seemed highly satisfactory. One of the fifty-nine patients died of sudden massive gastrointestinal hemorrhage from a peptic ulcer. No others died in the CCU. Two patients required resuscitation from ventricular fibrillation. Eight patients died after leaving the unit, one from cardiac arrest, five from heart failure and one from papillary muscle rupture and another from pulmonary embolism. Bradycardia responded to atropine in thirteen patients and heart block in two required transvenous pacing.

At the start of the trial of sleep treatment the authors were concerned that hypoxia and metabolic acidosis, shock, respiratory infection and pulmonary embolism might be complications, but only in one patient was any problem encountered during sleep treatment and this was a patient with pulmonary embolism, who had had multiple cardiac arrests which could hardly be attributed to the sleep per se.

The sleep regimen seems to be a safe and practicable method for treating acute myocardial infarction in a CCU where the personnel knows how to handle intravenous promethazine and pethidine and how to give intravenous atropine, lidocaine, and heparin when ordered. Use of amitryptaline (elavil) could make the sleep even easier to achieve. During the first days when the death rate from myocardial infarction is highest, the sleep treatment did favorably modify the natural history of the disease in the hospital without creating special risks and is certainly worthy of trial in a larger number of patients.

Whether or not further trials support the impression that sleep was a vital part of the regimen, this approach does provide the patient with the most pleasant introduction to life with cardiac infarction that we can think of. We know that pain and mental distress increases catecholamine secretion. We know catecholamines aggravate cardiac arrhythmias.[4,5] We know that deaths from electrical disturbances in acute myocardial infarction do occur. Now we know some of these can be prevented by sleep.

L.H.N.

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The National Conference On Coronary Care Units

Approximately 550,000 patients die each year of shock, heart failure or cardiac arrest. Of these 250,000 do not reach the hospital. Corday[1] believes that if coronary care units (CCU) were established across the nation 50,000 might be saved. The CCU concept then would appear to be a most important contribution to medicine of this decade. When these units were first established their primary purpose was to serve as resuscitation centers. An alarm can alert the staff to the onset of cardiac arrest. When authority to apply countershock was delegated to nurses up to 70 per cent of patients suffering arrest from ventricular fibrillation could be resuscitated. Here then emerged a new role for the nurse. She needed to be properly trained electrocardiographically and in skill to employ countershock.

The next step obviously was preventive. If antiarrhythmic medications are administered to patients with cardiac irritability then cardiac arrest becomes an unusual event. This new phase requires earliest recognition as well as signs of heart failure which must be treated vigorously. Soon we will be entering into a new phase—the pump assist. When applied extra-corporeally the pump has promise in the treatment of irreversible cardiac arrest, heart failure and the shock states. We need to know which of these are salvageable, however, since failure and shock are generally evidence of severe cardiac damage often incompatible with life regardless of the strenuous efforts that might be employed to combat these almost fatal complications.

It was time for leaders of the field, medical, nursing and hospital administrators to assemble and consider where we are and whither we are going in this expanding area of medicine. Already 350 hospitals throughout this country had set up CCU's even though the practice was scarcely five years old. Such a conference took place in June, 1967 in Washington, sponsored by the Public Health service and attended by 650 leaders from every part of this country. The areas discussed were experiences and problems in establishing CCU, the required facilities, equipment, personnel and their training for units of various size hospitals, experimental results and problems in the aggressive management of myocardial infarction (MI) in CCU, mutual problems encountered by physicians, nurses ,and other personnel who work in CCU. Finally there was stressed the need for research that will provide information on the prevention of the catastrophic complications of MI.

Like most conferences this one opened with a plenary session, followed by six simultaneous full day work panel sessions and a final plenary session, at which were summarized the deliberations and recommendations. Obviously they were based on current state of knowledge and experience with regard to CCU. But the field is expanding rapidly, and concepts are bound to change, and this made formulation of hard and fast rules and guidelines difficult to establish. What is permanent in our thinking, however, is that the CCU has opened a new day of promise for heart patients survival for relief of suffering and added a new dimension in health care.

What has been pointed up was what are the ingredients of good care and how hospitals can be assisted if they are having difficulties in achieving good results. Such results could be compromised if the monitoring is not perfect, if the nurses are inadequately trained and there is a shortage of trained nurses in a unit. Also broadly considered was the need to keep physicians abreast in the latest techniques. Emphasized was the seminar involving visiting physicians to work with CCU directors and training of CCU directors. The problem of obtaining effective surveillance in small hospitals of 50-75 beds in rural areas was considered and whether one hospital in an area be designated to handle all MI cases. Another matter considered was how to get patients in a hospital early when their arrhythmic tendencies might particularly warrant it.

It is clear that training of personnel is extremely important because CCU staff must be razor sharp to react accurately and swiftly. This means training for the instructor, the CCU supervisor and the entire CCU staff. At present it was noted that although 44,000 such skilled staff are needed around the country there is at present available 1-2,000 per year. Add to this the retraining program because last year's precepts and equipment become obsolete, and we get a glimpse of the immensity of the problem.

As the concept of CCU evolves so does the image of the nursing profession. The situation demands that nurses be trained to perform duties formerly reserved only for the physician. This requires highly motivated nurses. Already, however, this special role has strengthened the nursing profession and given it a new status. There are here medical and legal questions involved and the ad-

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justment of the whole medical profession. As more of the 7,000 hospitals in this country set up CCU, paramedical personnel will increasingly take on a new role in the practice of medicine.

The design of the unit was fully explored. It must provide more privacy because aggressive procedures can be a traumatic experience to a patient already gravely ill and fearsome. The present technique of making the patient visible at all times limits the size of the CCU to 4-6 beds. In most large hospitals it needs to be larger. The struggle for scientific management has led to the complaint that we are paying too much attention to the organ system, to the neglect of the whole individual. We must be considerate of the human side of patient care. It is claimed that the aggressive management of the patient with MI has already led to a fragmented pattern of depersonalized care and that this adds tremendously to the frustration and anxiety generally associated with illness.

There is much here to think about. The concepts which underlie the CCU is revolutionizing certain practices in nursing, medicine and the personal relation between physician and patient. The CCU, however, is an ideal demonstration of the expansion of health care, the rapid improvement in knowledge and concomitant growth of skill among physicians, nurses and other paramedical personnel. There are no longer any artificial lines of demarcation between the various groups. Some things the nurse can do better than others and also perhaps even pharmacists. There are appearing new levels in health personnel.

For many years medical educators and others have been said to suffer from "hardening of the categories." Now we are entering a period when we must innovate, experiment, and accept criticism and move forward to solve the health problems of the nation.

L.H.N.

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Mechanisms Of Abdominal Pain

The only pain that is easy to bear is the pain of others.—Réne Leriche.

Bockus[1] has rendered clinical science a service by drawing a working hypothesis or formula to explain mechanisms of the principle types of abdominal pain. In this way we may gain expertness in bedside diagnosis. First of all he emphasizes that there is such a thing as true visceral pain although for ages this was denied. The statements that cutting into the brain or liver or abdominal viscus without causing pain is extent in the literature but is not valid in the light of recent physiologic studies. Fortunately pain nerve endings are few compared to what is found in the skin. We know now that they are stimulated by motor changes in the viscus—contraction or distension. Anoxia and changes in the vascularity can also produce visceral pain.

There are now recognized three major categories of pain arising in abdominal viscera: true visceral pain, referred pain and peritoneocutaneous reflex pain. The exact mechanism of referred pain is not clearly understood but occurs if inflammation has taken place. In this instance there is skin hyperalgesia, muscle, guarding and local tenderness.

Once the parietal peritoneum becomes involved it causes the pain to be referred to the overlying integument through direct activation of central nervous system pathways. This reflex is entirely by way of somatic nerve endings. This is the most intense pain and is characteristic of peritonitis—"the acute surgical abdomen." There is present spasm, rigidity of the abdominal wall and intestinal paresis—"a silent abdomen."

The appendix can be used as an example. The first pain is periumbilical—true visceral type. The second pain is in the lower right quadrant—the referred type. The third pain is in upper right quadrant—peritoneocutaneous pain. In the absence of a careful history detailing the occurrence of the first and second types, an erroneous diagnosis of a ruptured gallbladder or duodenal ulcer may be made.

Once a diagnostician adopts this sort of tentative formula to explain the abdominal pain mechanism then he requires a further appraisal of the patients pain threshold, his reactivity both physiologic and psychologic. He needs to remember that nothing short of the whole person participates in the pain experience. Psychological aberrations influence pain perception sometimes to exaggerate it and at other times to disguise it entirely.

Older patients may have dulling of the pain stimulus so that we need to be particularly cautious in the interpretation of symptoms in some older patients. Iatrogenic factors such as sympathectomy may be responsible for the absence of the pain as

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*As shown by *in vitro* studies.
1. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. *65*:311 (Feb.) 1953.

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a warning signal for here afferent visceral fibers accompanying the sympathetics were severed. As a result true visceral pain in that neural segment cannot be registered. Anti-cholinergics in large doses dull the effect of a stimulus that might be caused by contraction and dilatation of a viscus-type one, pain. Anelgesics when administered too soon and in too large doses eliminate the pain signal.

There is really no good method to evaluate a patient's pain threshold—that is the minimal stimulus capable of being perceived. Skin pain may be different from visceral pain. And it is also difficult to evaluate a patient's reactivity. Threshold seems to vary from person to person and perception of it may vary in the same person from time to time. Distraction, concentration on something else can raise threshold. Hypnosis and analgesics are threshold raising factors. Pain may become more intense in association with apprehension and anxiety.[2] Anticipation of pain also lowers threshold. So does inflammation and congestion lower threshold through vasodilatation and kinin liberation which activate chemoreceptors.

The patient's intensity of reaction to pain, that is his suffering, may be closely related in many instances to what the pain means to him. Severely wounded soldiers when taken from the front-lines are relieved from tension and fear, bear their pain more easily. Postoperatively a patient can better bear his pain knowing the worst is over and his recovery is assured. The psychological processing of the sensation has as great importance in the appreciation of pain as the intensity of the stimulus. With this fact in mind the good clinician will find the appropriate case on which a sedative will work as well as a narcotic.

We must remember that pain is the central problem in medicine. Without pain there would be little in medical science and almost no doctors. It can be beneficent because it brings the patient to the doctor. Every pain has its distinct and frequent significance if we will but carefully search for it. That patient is lucky when he finds a physician who has a good understanding of the clinical aspects of pain mechanisms and their vagaries. Such a physician's diagnostic acumen is more closely related to expert clinical appraisal than it is to the interpretation of laboratory data. He will go to the laboratory but only after a careful historical and clinical analysis.

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Genetic Damage From Chemicals: I. Nitrites And Nitrosoamines

Is genetic damage from chemicals the number one health problem? There are thousands of chemicals to which humans are normally exposed. A growing number of geneticists share the view that genetic damage from ordinary chemicals may be one of man's most urgent health problems. This threat has been called the submerged part of the iceberg of genetic risk as compared with radiation damage. It is our number one health problem.

Potentially irreversible damage might be done without warning by some of the more than 1,000 natural and synthetic chemical substances produced commercially or by the million or more others that have been isolated or synthesized. Fewer than 200 of all these suspected mutagens have been systematically assayed and none has been definitely implicated, or cleared as a direct threat to man's future but now an editorial in Lancet tells us some rather extraordinary things on at least one kind of chemical, the nitrites.[1]

For centuries meat has been preserved with rock salt. The origin of this practice is unknown but after many observations it turned out that it was the metallic nitrate impurities of the rock salt that had reacted with the meat pigments to produce its red color. To produce a uniform red color nitrates became uniformly employed together with the salt. The nitrate is reduced to nitrite by microorganisms and so the next step logically was to substitute nitrite for nitrate in the original salt mixture.

The chemistry of the curing process is complex and is based on reaction between sodium and potassium nitrite and myoglobin and hemoglobin with the formation of nitroso-hemoglobin and nitroso-myoglobin which are the red pigments. Nitrites are used in many countries and they have an especially valuable preservative action against clostridia. This use is permitted in cured and pickled meat products and in some cheeses.

The acute and subacute toxic effects of nitrites are well known: vasodilatation, lowering of blood pressure and formation of methemoglobin. Babies are particularly sensitive to nitrites because fetal hemoglobin is more readily oxidized to methemoglobin than is adult hemoglobin. This sensitivity had led to fatal methemoglobinemia in babies who have been given well water containing nitrates which can be reduced to nitrites by the microbial flora of the gut. Even in adults who take nitrates for coronary artery insufficiency, it is good practice to administer this drug on alternate weeks to prevent accumulation of methemoglobin.

Nitrates are present in several vegetables and samples of spinach used as baby food may contain considerable quantities. Some of this nitrate may be reduced to nitrite during preparation of the baby's food and this has sometimes led to methemoglobinemia. This aspect of nitrate toxicity has been taken into account in regulating the use of nitrites in food, but the situation has become remarkably more complicated since the discovery of the remarkably toxic carcinogenic and other biological actions of the nitrosoamines, because under certain circumstances these compounds may be formed by the interaction between nitrites and secondary or tertiary amines.

The first discovery was that dimethylnitrosoamine has hepatotoxic and carcinogenic actions. The nitroso carcinogens are extremely potent and are active in a wide range of species inducing tumors in virtually all organs of the rat and they have the remarkable capacity to induce cancer after only one dose. These compounds are also teratogenic and have induced tumors in the progeny when given to pregnant rats. Clearly, then, the possible occurrence of these biologically highly active compounds in food or other environmental situations is a matter of the gravest concern. In Norway the incidence of liver disease in ruminants was high when they were fed meal from herring preserved with sodium nitrite and this suggested that nitrosoamine had been formed. Similar experiences were found in sheep and mink.

Nitrosoamine can be formed from nitrites even when food is stored at 2-4° C. and feeding of even 2 ppm. in the diet in rats produced 7 per cent of liver tumors. Nitrosoamine may be found in other environmental situations. They have been detected in minute amounts in cigarette smoke. It is even uncertain whether or not it is present in white flour. If man is sensitive to nitrosoamine carcinogenesis and there seems no reason to assume that he is not, the implications of the above observations are obvious. Nitrosoamine can be formed in vitro from secondary amines and nitrate when mixed together in human gastric juice. This formation of n-nitroso compounds by nitrosation of amines might very well happen in the human stomach.

Apparently, therefore, carcinogenic nitrosoamines could be formed by interaction of nitrites with amines present in food and hazardous levels might be attained in foods of high amine content. Any possible risk to human health arising from the addition of nitrites to food must, however, be balanced against their value as preservatives especially their action against clostridia. Nitrites however taken in food or therapeutically must still be held suspect.

The diabetic antibiotic streptozotocin isolated from streptomyces achromogenes is a nitrosoamide and induces kidney tumors in rats. This compound seems to be the first known naturally occurring nitroso carcinogen, but a related series of natural carcinogens found in cycad plants has been well investigated since their carcinogenic action was first reported five years ago. The plants are widely distributed throughout the tropics and subtropics. Other carcinogenic compounds exist with biological and biochemical actions virtually identical with those of the nitroso compounds. Some have been isolated from strains of streptomyces and others from fungi that produce aflatoxin. These are widely distributed organisms and the possibility that they too can contaminate food must not be dismissed.[2]

L.H.N.

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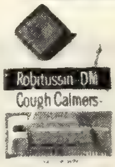

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Foreword

The purpose of this special issue in *Connecticut Medicine* is to focus the attention of the members of the medical profession in Connecticut on the changing attitudes and patterns of medical practice as they relate to the general practitioner.

In all aspects of human existence we are passing through a period of transition. Enormous dynamic forces are at work affecting both social and medical changes and much of the way in which the future is shaped will depend on how much thought we, as physicians, give to these problems. Whatever form these changes take they must embody the essence of medical philosophy that encompasses the best interests of the patient.

The more we study the plight of our family physician, the more insight we develop into all branches of the practice of medicine. The changes in general practice apply to all fields, for each branch of medicine reflects the standards and coordinated efforts of associated specialties.

In the following pages an effort has been made to consider whence we came, where we are, and where we are going in the practice of medicine particularly with the intent of preserving the personal relationship between the physician and his patients. Our contributors will review and discuss family practice. Their material is sub-divided into the preparation, function, continued education, self-appraisal and future of the family physician. We urge our members to actively participate in the consideration of these matters and to communicate with each other in the correspondence section of our *Journal*.

WALDO E. MARTIN, M.D.
Guest Editor

The Future of General Practice

George E. Burket, Jr., M.D.

"The general practitioner is dead and buried and is to be forgotten" is the contention of some while the Millis Commission, the Folsum Commission and the Willard Committee all support the concept that the primary physician, the personal physician, or the family physician must be produced in increasing numbers. Faced with these divergent opinions one would think that the future of general practice would be hard to predict, but indeed it is not if one is perfectly knowledgeable concerning the area of general practice and is willing to make a realistic assessment of the facts. The real difficulty is approached when one attempts to discern what this area of medicine will be called in the future, what new roles will be assigned to it with adequate research in the delivery of health services, and what form the training program will take when the academic world comes to a full realization as to what human beings need for total health care.

First of all let's take a good look at the proposition that general practice is dead and buried. No one can deny the fact that the number of general practitioners registered as such with the American Medical Association have decreased in the past thirty years from 120,000 to 70,000. Also, one must face the fact that in a similar length of time medical school graduates, indicating that they are going into general practice, have dropped from 60% to less than 15%. But let's consider figures further. The American Medical Association's latest publication on Distribution of physicians, Hospitals, and Hospital Beds (1967) lists 102,000 physicians in the general specialties, i.e. general internal medicine, general surgery, general pediatrics, and obstetrics and gynecology. A safe estimate would place the number of these general specialists who are doing general practice at 50,000. Add this figure to the 70,000 and we are right back to the 120,000 figure of thirty years ago.

I think it also significant to point out that according to a recent American Medical Association survey the number of full time specialists participating in multi-specialty groups has gone up in the past seven years from 10,081 to 13,814 to reach a percentage of 7.6 of the total number of physicians in private practice or an increase over the 7.1% of seven years ago of .5%. This could hardly be considered an earth shaking change in view of the rush to specialization by medical school graduates in the past twenty years. This then would seem to indicate that the majority of those trained in specialties are either practicing solo or doing general practice. Somewhere along the line certain undertermined number of the 85% of medical school graduates who indicate they are going to specialize end up doing general practice while claiming a specialty.

Why does this happen? The answer is simple and obvious. Young physicians feel forced to do this by false educational and social concepts and rules placed upon them by organized medicine and perhaps to some extent by an improperly informed public. They claim a specialty while doing general practice in order that they might have hospital privileges, status, and in many instances, some type of a definite, well-recognized training pathway to follow.

Thus, we have developed a system in the United States in which we have large numbers of unidentifiable general practitioners. Unidentifiable to prospective patients seeking entrance into our health care system and unidentifiable to organized medicine which no longer can really identify its parts. General practice is not dead. Part of it is merely submerged. Furthermore, many of these physicians are performing in areas where they have had no formal training. This would not be necessary today if in the past twenty years there had been developed proper number of graduate training programs in general practice. All of this, I am sure everyone will agree, is not in keeping with Medicine's quest for excellence. Our system is defecting our own goal.

In recent years with the three reports previously mentioned and their recommendations for primary, and family physicians well in mind, Medicine has finally come to realize the importance of this area of medical practice. Difficulties have arisen in moving forward because many in influential posi-

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tions, in academic and clinical medicine, are trying to solve the problem by staying on the same conventional track we have been following for thirty years. They are advocating training more and more specialists in depth to be utilized in groups to fill a void that could best be served by one man trained properly in breadth. This is like trying to fit a square peg into a round hole. It just will not work.

Our problems are compounded at present by many of the social planners who are so effective in influencing government health care programs and medical education, but who have very little knowledge of the actual delivery of total health care or the potential of the family physicians in the health care spectrum. Many of these planners are also trying to fit the square peg in the round hole and their recommendations have a profound effect in directing government resources.

Evidence that we are making very little progress, traveling down the one narrow road, is made more clear when one realizes that in 1967 the United States spent 40 billion dollars for health care without definite indications of better total health benefits. The frightening thing about the failure of our present system of educating and distributing physicians is the intimation in some quarters that there, of necessity, be more and more government control. The unsuccessful $5,000,000 program in social medicine seems to be followed by a $10,000,000 similar endeavor and in many instances the lack of success is blamed on the private sector of medicine's unwillingness to cooperate. In reality the private sector's advice is often times ignored.

The bright side of all that is occurring at present is the fact that individuals in influential positions, charged with responsibilites in medical education and in social planning, are becoming aware that our present dilemma, which has developed over a period of years, parallels the decrease in general practitioners or personal family physicians. This is undoubtedly not the sole factor involved, but it is now recognized that it has had a part in our difficulties in delivering total health care. The realization is spreading rapidly that physicians trained to practice comprehensive, continuing medical care as family physicians must be delivered to the health care system in large numbers. The United States has the potential for the best health care in the world. The thrust provided research by specialization has produced this potential. Family physicians must now be trained in greater numbers to serve as catalysts in delivering this service to people.

For twenty years the American Academy of General Practice has been calling for the education of more physicians for this area of medicine. For almost seventeen years the Academy's words and warnings fell on deaf ears until suddenly the realization came that something was wrong with the delivery of health services.

Three national commissions were activated and after thorough study of the problem for two to three brought forth the solution—more family or personal physicians specifically trained and certified for this function. Two of these commissions made several other recommendations but this one suggestion has occupied the spotlight and has had the most profound effect. The American Academy of General Practice now finds itself with many strong allies in this endeavor.

The Willard report (ad hoc committee on Family Practice) recommended that family practice be recognized as a special area of medicine and that there be created Family Medicine departments in medical schools with model family practice programs. This report also stated that the graduate program for this area of medicine be of three years duration and that a primary Board of Family Practice be formed to certify physicians completing this training. This ad hoc committee was composed of representatives from the Association of American Medical Education of the AMA, the American Academy of General Practice, and the section on General Practice of the AMA.

Stimulated and guided by the Willard Committee report, the Commission on Education of the American Academy of General Practice after conferences involving one hundred twenty-one medical educators produced a new graduate training program for family practice. This program is entirely new in concept, eliminates total block curriculum, is comprehensive throughout, and simulates actual family practice.

The American Academy of General Practice and the Section on General Practice of the American Medical Association now has on file the final application for permission to form an American Board of Family Practice. This application was considered by appropriate bodies representing the Advisory Board of Medical Specialties and the Council on Medical Education of the American Medical Association in February, 1968. Decision on the application by these bodies was deferred pending modification of the application. Conferences have now been arranged to make the recommended modifications and eventual approval is anticipated.

Most of the total opposition to such a Board seems to have subsided through proper communication and understanding.

Many community hospitals are ready to begin family practice training programs and several medical schools are prepared to plan family practice programs when certification is established. Approximately eight medical schools already have family practice programs underway.

Personal communications and letters indicate hundreds of medical students are now interested in family practice and are quite knowledgeable concerning the need in this area of medicine. They also seem to recognize the satisfaction to be derived from being a family physician. The Student American Medical Association in 1967 want on record as favoring education in family medicine and board certification.

Many do not realize the relationship between general practice and family practice and perhaps a few words should be written about it here. The physician we are referring to in this discussion is not the old family doctor of the early twentieth century anymore than the surgeon of that era is the surgeon of today. There is a conceptual difference between general practice and family practice as is well stated in the Willard report. However, most general practitioners do family practice and for this reason they are often considered the same and sometimes the terms are used interchangeably. In the past the general practitioner has not been trained as a family physician but becomes one through a definite process of self education during practice. The family physician of the future will be the general practitioner formally trained in family medicine.

For those of us in general practice today this evolution will hardly be noticeable except that we will feel great pride in the increase in the numbers of bright young physicians entering the area of practice with which we are so familiar. It will bring forth a fine new future for the medical student of today, the family physician of tomorrow, and the health care of the American people.

All of Medicine will profit in that more identifiable physicians will be produced through whom people may find their way into our health care system and remain there. Other specialty areas will once again assume their rightful place in Medicine as physicians highly trained in depth in their specialty—physicians trained completely in the sophisticated knowledge and skils which are certain to increase in the future and to whom patients can be referred with complete confidence when this knowledge and these skills are needed.

When one examines the actual needs of the American people for health care and recognizes that traditional barriers to education for the general practitioner and family physician are beginning to be removed, one can only predict an expanding and challenging future for this area of medicine.

"What is hard to bear is the complacent indifference with which the medical profession often regards issues, including issues of war and peace which are beyond its immediate purveu. It is nonsense that doctors whose professional concern is with preserving life, should not be personally committed to preserving peace"—Leading Article: After Essex. Lancet I: 1133, 1968.

It Won't Happen by Chance

A paper on Continuing Education of the Family Physician

Arthur D. Nelson, M.D.

> *May there never develop in me the notion that my education is complete, but give me strength and license and zeal continually to enlarge my knowledge.* —*From Maimonides' Daily Prayer of a Physician*

As far as recorded history is concerned, Plato, who probably overheard it in a bar, first wrote, "Education is a lifelong business." This holds particularly true today for the learned profession of medicine. As defined by Webster, a profession is "a calling requiring specialized knowledge and often long and intensive academic preparation." In Russia, young physicians take an oath to continue the study of medicine and increase and improve their knowledge. Our own Hippocratic Oath encourages physicians to honor their teachers, but is strangely silent on the need for continuing education. However, all of us agree that maintenance of skills must be the constant concern of every physician. High standards of patient care can be achieved only if the knowledge applied is up-to-date.

The difficulty of keeping current varies directly with the amount of information available for assimilation. The explosion of knowledge caused by the Herculean research efforts we have seen over the past 25 years has "blown up" the size of the problems facing us today. Unfortunately, the existence of new knowledge has not always led to the application thereof. Public Law 89-239, known as the "Regional Medical Program", was passed because of the need to shorten the delay in applying the fruits of research to patient care.

Public sentiment for the relicensing of physicians reflects further concern for the gaps between what is known and what is applied. The report of the National Advisory Commission on Health Manpower, for example, suggests that professional societies and state governments should explore the possibility of periodic relicensing of physicians and other professionals. It goes on to recommend that relicensure should be granted either upon certification of acceptable performance in continuing education programs or upon the basis of challenge examinations in the practitioners specialty.[1]

Call it what you will, threat, compulsion, or inducement, this recommendation suggests a determination on the part of society to have the best of what is known. A paradox exists, however. The new information is already available to the practitioner, but he isn't getting it under existing conditions. There is no shortage of opportunities for continuing education. For example, the *Journal of the American Medical Association* describes 1,830 courses offered by 387 institutions and organizations for the period from 1 September 1967 through 31 August 1968.[2] Many of these courses will be attended. However, this extensive listing is a reflection of effort, not accomplishment. Many teachers will expound on many subjects; how much knowledge will be transferred is a moot question. There is no convincing proof that the work involved in preparing and delivering all these continuing education courses results in universal improvement in actual patient care. The courses are usually set up by well-meaning medical educators who arbitrarily decide what the audience ought to know, without consultation with or even identification of the target physician population. The relevance of the material to the needs, interests and motivation of the practitioner is often questionable. Even if the information is pertinent, the quality of pedagogy employed (usually lecture) often defeats the purposes of the presentation.

Perhaps because available offerings do not meet the needs of the practitioner, relatively few take advantage of these opportunities to continue their education. For example, in response to a survey by the State Board of Medical Education and Licensure in Pennsylvania, only 25% of physicians reported they had attended a post-graduate educational course within the past two years.

Physicians give a number of reasons for their failure to attend courses. They express reluctance

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to leave their patients unattended. They also complain about poor timing of courses, inaccessible locations, and inappropriate subject matter of the material to be covered. The expense of attending, coupled with loss of practice income, must also be deterrents. Thus, apart from a personal drive for complete competence in his calling there seem to be few inducements and many inhibitions affecting the individual in solo practice desirous of participating in formal programs of continuing education.

If we agree that educators and practitioners don't seem to be getting together, we must inquire how these communication gaps developed. On the one hand, it is possible that medical educators have lost sight of their basic objective, to educate adequate numbers of practitioners of medicine. It does seem just possible that they are concentrating much of their energy in training undergraduates, interns, and residents in their own image of teacher and researcher. When the primary goal is fuzzy, it is not surprising that the secondary goal of maintaining the skills of graduate practitioners is also compromised. The last great upheaval in medical education followed the publication of the Flexner Report in 1910. The present medical establishment is now in its third and fourth generation; little more than evolutionary change has occurred in recent years. Secure in their ivory towers, nurtured by generous legislators, either directly or through research grants, educators have become conservative traditionalists.

On the other hand, the practitioner should not leap to throw the first stone. The town-gown syndrome which reflects a schism between educators and practitioners is most often generated by the practitioners' fear of competition by the academician. Thus, the private practitioner must share responsibility for an artificial limitation on the educators practice which makes it atypical of real life. The polarization resulting from conflict of interest makes it difficult to creat community of interest in continuing education. Small wonder the groups have drifted apart.

With a few notable exceptions, there has been an absence of active leadership by academicians in continuing education. The only alternative has been a do-it-yourself operation by practitioners, their hospitals, and their professional societies.

Of all these organizations, the American Academy of General Practice has demonstrated the most vigorous leadership in encouraging its members to maintain qualification in their field. Membership in the Academy can be renewed only upon presentation of evidence that the individual has attended post-graduate courses or undertaken activities which reflect continuing study on his part. Now, the Academy is introducing the concept of a challenge examination, the successful passage of which would permit the individual to be certified as having special skills in the field of family practice. This is part of the proposed certification process described in the Academy's application for a certifying board in family practice. The application also reflects the Academy's desire to recertify members every six years through the medium of additional challenge examinations.

If, as professionals, and specialists and members of the American Academy of General Practice, family physicians must maintain competence, the basic question is, how can this best be done? As John Galbraith has said, "The inevitable counterpart of specialization is organization."[3] This, perhaps, is the answer to our dilemma.

We should note the successful results of organization in fields other than Family Practice. For example, professionals in the General Electric Company or scientists at General Motors have very little difficulty with their continuing education. Professional development opportunities are built into the structure of their corporations, permitting scientists to maintain supremacy in their fields. Strong universities and medical schools provide similar upward tracks for their faculty members. Organization may well provide the mechanism for self-improvement and advancement for family physicians.

The continuing education component of a neighborhood health center program being initiated by Temple University will serve as an illustration. The center will have as its backbone a group of primary physicians recruited from the ranks of general practitioners in the neighborhood. Because of isolation, many of these physicians have had difficulty in the past in maintaining their fund of information. In the structured organization of a relatively large group practice, we expect to obviate some of their problems. Each module of physicians will have a pediatric and internal medicine consultant as a member of the team. The family physician will work up every patient, will define the problems, and will have a personal interest in seeking the best solutions. Thus, he has motivation to learn from these specialist consultants, whose primary mission is to serve the staff physician and only secondarily, the patient. Staff conferences and internal audits will provide other opportunities for continuing education. Furthermore, in an institutional setting, staff appointment, faculty rank, peer recognition, financial reward, and other emoluments can be both inducement and reward for physicians who know they will be judged on the basis of performance. The opportunity they will have to teach and lead can provide additional motivation for study and research. To assure full opportunity for these activities, about 25% of a physician's time is actually scheduled for other than patient care.

There is ample evidence to show that the average patient is incapable of judging quality of care. Peer evaluation is quite another matter. In an organizational setting, evaluation, quality control, establishment of standards, in fact, full accountability for professional endeavor, can become part of the physicians daily life. It not only can, it must.

Affiliation with an academic institution also makes education outside of the immediate group both available and attractive. Formal course work, conferences and symposia, and library of clinic research are all there for the asking. They can be described as passive resources of the institution. However, active personal involvement with dynamic resources of the university can be achieved by assigning family physician members of the neighborhood health group to the staff and teaching services of the University Hospital. All patients referred from the neighborhood center will be followed by their family physician, and by consultants from the teaching staff also. This system should result in optimum care for the patient, relevant education for the family physician, and contact with a real-life practitioner for the specialist consultant.

Where educators and researchers do not practice, and practitioners may not teach, or in fact, come into contact with the other two, it is easy for the two groups to drift apart. This problem might easily be avoided if the protagonists in this common conflict could be permitted and encouraged to change roles from time to time. This is indeed part of the plan at Temple University. Not only will Neighborhood Health Center staff members come into the main center, but on a rotating basis members of the faculty of the schools of the center will be encouraged to move out into the neighborhood centers for a participant's view of the actual needs and health care demands of a defined population group. Hopefully, such excursions into community practice will enable the researchers and teachers to increase the relevance of their academic endeavors, while performing the equally valuable function of bringing the latest knowledge to the point of delivery to society. This plan to incorporate continuing education into the basic organization of our center makes the latest information in the form of problem solving help constantly available to every family physician in the group. Finally, on the assumption that seduction produces consistently better results than compulsion, we plan to incorporate a professional reward system which will relate compensation, promotion, and assignment to the results of medical audit and evaluation of performance. Every member of the staff can look forward to advancement based on his own ability and willingness to grow. We hope and expect that the results of this program will be personal satisfaction for the professional and superior care for the patients.

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Preparation for Family Practice

Lynn P. Carmichael, M.D.

That a physician should be specially prepared for family practice is a new concept and this preparation has been the concern of three nationally constituted commissions. These were the National Commission on Community Health Services, The Citizens Commission on Graduate Medical Education and The Ad Hoc Committee on Preparation for Family Practice. All three of these groups, the Folsom, the Millis and the Willard Commissions, reported in 1966. They all agreed that there exists a need for a specially trained physician to render comprehensive family health care. These three reports undoubtedly will have a significant effect on the medical care services of the future and should be read and studied by all health professionals.

There has been some confusion about the terms "family medicine," "family practice," and "general practice." Many have used these terms interchangeably but I feel that significant differences exist. Family Medicine has been defined as that branch of medical science that has as its responsibility the continuing health maintenance of the family. This definition establishes Family Medicine as a discipline or a specialty having a distinct composite body of knowledge. As an academic discipline Family Medicine belongs in the University setting and knowledge in Family Medicine can be obtained by not only physicians but nurses, social workers, sociologists and all other members of the health professions.

Practice on the other hand is what the physician does in the community. Implicit in his practice are social, political, economic, geographical aspects. A physician who goes into the community and devotes himself to the episodic care of diseases is in general medical practice. A physician in the community who offers continuing health care to families is in family practice. This would not mean that he necessarily limits himself to the practice of Family Medicine. In addition to Family Medicine he may practice obstetrics, pediatrics, dermatology, or any other medical specialty. It is the interests of the physician and the needs of the community that should determine what his practice will be.

Only recently have programs been developed to prepare physicians for family practice. While there have been general practice residencies most of these programs have been nothing more than an extended rotating internship and the relatively few programs have attracted even fewer physicians. This does not mean that there are not fine family physicians throughout the United States. Many general practitioners have become excellent family physicians just as have many internists and pediatricians. This transition from general practitioner, internist or pediatrician to a good family physician has depended upon experience gained in practice. The general practitioner has been unprepared for this role and the pediatrician and the internist, while well trained, have been trained in the wrong things. The public as well as the physician suffers when a physician's education depends upon self-teaching and self evaluation.

The Division of Family Medicine, of the University of Miami School of Medicine, has developed an integrated undergraduate and graduate training program for family practice. The Division of Family Medicine offers instruction in family medicine to medical students, interns, and residents with additional training necessary for family practice being given by the other clinical services. Each medical specialty requires a certain setting and specific materials. The surgeon requires an operating room, a knife and a patient; the clinical pathologist needs a laboratory bench, various chemicals and a specimen; the obstetrician needs a delivery room, an expectant mother, and a tub of hot water. Family Medicine cannot be taught in the laboratory, operating room, or hospital bed. For training in family medicine to be given there must be an ambulatory care facility and the opportunity to develop a continuing relationship with families. The heart of the training program at the University of Miami is the Family Health Center.

At the present time aproximately 200 families are being cared for at the Family Health Center. While there are a few extended families with one or more set of grandparents, most are nuclear families. In several cases there is no father in the home because

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of death or separation. The families generally are not indigent and present a wide range of socioeconomic and other characteristics. Only a few families have dropped out of the program due to dissatisfaction.

Three separate phases of the training program can be identified. The first is the student family health service. This is an extension of the University's student health service and provides family health care to the medical student and his dependents with professional courtesy being extended. The objectives of the program are:

1) To provide high quality care for the student and his family.
2) To demonstrate to the student what comprehensive health care is by making him and his family the recipients of this care.

The care in the Family Health Service is given by the attending staff of the Division of Family Medicine. These men are all seasoned physicians and practice in the community. They come in on a once-a-week or once-every-other-week schedule and continuity of care between the physician and the student family is attempted. We estimate that 25% of the students have availed themselves of this service.

The second phase is the undergraduate program. This is an elective open to the medical student when he finishes his second year. The objective of the program is not to teach the student the knowledge and skills required in family practice but to encourage the student to develop and maintain positive attitudes towards caring for families. Each student who elects the program is assigned a family and he serves as their family physician for the next two years under the close supervision of the program staff. We attempt to assign the student a family in which the mother is expecting. This provides sufficient contact between the student and the family.

The first year we offered the program 18 students signed up for the program and 10 were selected. In the next year (class of 1968) 24 students elected the program and 15 of these have continued into the senior year. This year 60 students out of the 80 in the class of 1969 signed up for the program. We will not be able to take all of these students into the program but we hope to find families for at least twenty.

The graduate ,training program is the third phase. The objective of this program is to prepare the physician for family practice. In the Family Health Center he gains knowledge and develops the skills of a good family physician. Through assignments to the other clinical services he develops competency in these areas.

We offer a one year rotating internship as the first of the three year graduate training program. Each intern spends one day per week in the Family Health Center caring for the 10 to 12 families assigned to him. His in-hospital rotation consists of 4 months of internal medicine, 4 months of pediatrics, 2 of obstetrics and gynecology and 2 elective. Six positions are available and last year there were over 50 applications for these six positions.

The residency is a two year approved program. Each resident spends one-third to one-half of his time in the Family Health Center caring for families assigned to him. The resident is expected to build up a case load of approximately 50 families. He participates in the teaching of the interns and students. In addition to his assignment in the Family Health Center, over the two year period he will spend 9 months in internal medicine, 6 in pediatrics, 3 in mental health, 3 in public health and 3 elective. This year we have four residents and next year we have requested this be increased to seven. The supervision of the interns and residents is given by the same attending physicians who come in to care for the student families. Teaching is, therefore, by practice and example.

In addition to the clinical teaching there are the following conferences. There is a separate weekly family medicine conference for the third year class, the fourth year class, and the physicians in the graduate training program. These conferences usually have as their topic some aspect of ambulatory practice and are quite well attended. Frequently guests are invited to participate in the discussions. There is a weekly seminar on the Physician-Family Relationship conducted by a psychiatrist with analytical experience. This seminar focuses on the physician's contribution to the doctor-patient relationship in an effort to strengthen the skills of the interns and residents in this vital area. The success of these conferences is due to Dr. Alberto de la Torre, who conducts the session.

The major teaching vehicle of the Division of Family Medicine is the weekly Clinico-Prospective Conference. At this conference one of the interns or residents presents a patient for whom he is caring and an individual health hazard appraisal is made. This is an assessment of this individual's risk of dying in the next ten years as compared to the average individual of the same sex, age and race. When this has been done the various measures that can be used to improve the individual's risk are discussed. Frequently an expert in a particular disease or system is invited to discuss the diagnosis, treatment and prevention. The emphasis is then on protecting the individual's and family's health as it is in most medical teaching exercises such as grand rounds or clinico-pathological conferences.

I have described an apparently successful graduate and undergraduate training program in Family Medicine. The heart of the program is the care of families in an ambulatory care facility, the Family Health Center, in which continuing comprehensive health maintenance of the family as a unit of living is emphasized.

ACUTE CORYZA.—Acute catarrhal inflammation of the upper air-passages, popularly known as a "catarrh" or a "cold," is usually an independent affection, but may precede the development of another disease. It prevails most extensively in the changeable weather of the spring and early winter, and may occur in epidemic form, many cases developing in a community within a few weeks. These outbreaks are very like, though less intense than the epidemic influenza, cases of which may begin with symptoms of ordinary coryza. The disease probably depends upon a micro-organism. Irritating fumes, such as those of iodine or ammonia, also may cause an acute catarrh of the nose. Many cases are so mild that the patients are able to be about and to attend to their work. If there are fever and constitutional disturbance, the patient should be kept in bed and should take a simple fever mixture, and at night a drink of hot lemonade and a full dose of Dover's powder. Many persons find great benefit from the Turkish bath. For local treatment, particularly in the early stage, when the mucous membrance is swollen and there is a distressing sense of tightness and pain over the frontal sinuses, cocaine is very useful and sometimes gives immediate relief. The four per cent solution may be injected into the nostrils, or cotton-wool soaked in the solution may be inserted into them. Later, the snuff recommended by Ferrier is advantageous, composed, as it is, of morphia (gr. ij), bismuth (ʒ iv), acacia powder (ʒ ij). This may occasionally be blown or snuffed into the nostrils. Coryza is rarely serious in itself, but renders the subject more susceptible to other affections. The attacks should therefore never be slighted, and in young children and in the old especial care should be taken during convalescence. The patient feels indisposed, perhaps chilly, has slight headache, and sneezes frequently. In severe cases there are pains in the back and limbs. There is usually slight fever, the temperature rising to 101°.—Osler, W.: *The Principles and Practice of Medicine*, New York: D. Appleton & Co., 1892, pp 474-475.

The Function of the Family Physician

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In association with changes that have occurred in medical knowledge and in the family, medical care for the majority of the American people is becoming more and more episodic and fragmented. People talk monotonously about the increasing technology, knowledge explosion, and specialization characteristic of modern medicine and the growing youthfulness, greater mobility, and earlier childbearing of the present-day American family. But, the development of an integrated body of knowledge which can provide a sound basis for the delivery of modern medical care to them is missing. Although recent reports have called for a personal, primary, or family physician,[1-3] there is some evidence to suggest that these reports and the proposal to organize a Board of Family Medicine are encountering opposition[4] and have not yet produced the needed favorable response in medical schools. Medical educators have proposed solutions to the delivery of health care which usually include hospital based specialty group practice and the development of larger numbers and new kinds of allied medical personnel. This represents a practical solution since the body of medical knowledge will continue to increase as will the numbers of specialists. The questions must be asked whether, in the face of increasing specialization, there is a unique function for the family physician or if there is a discipline of family medicine that should be practiced by all physicians no matter what their specialty?

Family Medicine has been defined as comprehensive medical care in which the physician accepts continuing responsibility regardless of the age of the patient . . . and recognizes a relationship of continuing patient management as pertains to the individual, his family, and his environment.[5] Many medical educators see this as a definition which seeks to replenish the ranks of the general practitioner. Feeling that no one physician can do everything, the function of the family physician in a health care system is not seriously considered.

The family physician is a health practitioner and should deliver health care which is continuous as well as comprehensive. This means that he must fully utilize the resources of the community, provide care in his office, in the patient's home, or in the hospital. He should be available when his patient is well and at times of crisis, and thus combine curative and preventive care. This physician does not wait for patients to come to him but reaches out and identifies the vulnerable patient, who, like the at-risk infant, is in a presymptomatic and asymptomatic stage of his disease. This family physician is not so different from the Chinese physician who was rewarded only when his patients were well. The family physician is knowledgeable about the family, and understands the different behavior demonstrated by patients who are sick and well,[6] because a considerable part of his training will have been in the behavioral sciences. He is experienced in psychiatry, pediatrics, and internal medicine, but only so far as this makes it possible for him to manage common medical problems and recognize uncommon ones. His expertise with disease enables him to manage common diseases well. He knows what good surgery is so that he can advise his patients but more than likely will rarely perform surgery himself. His body of knowledge will make him an expert at interviewing and in performing physical examinations, skills he will always use. He can be a marriage counselor, can recognize and advise regarding learning disorders, and use his relationship with his patients to manage chronic diseases and plan rehabilitation. He is more of a psychiatrist and more of a social scientist and less of a specialist in unusual disease. He is an expert in the technique of obtaining a consultation and knows how to select and use his consultants.

Many, no doubt, scoff at this description, which is only partial, as not being medicine. However, a close examination of what physicians are presently doing would suggest that this description is not totally imaginary or entirely in the future. Perhaps as many as half of the visits to a physician's office are uncodable by present coding systems. Pediatri-

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The Family Health Care Program has been supported by grants from the U.S. Children's Bureau, Department of Health, Education and Welfare; the Commonwealth Fund, and the Family Health Foundation of America.

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cians, trained in meningitis and in exotic metabolic diseases, leave practice for what seem to be greener pastures when they are actually faced by well babies, behavior disorders, upper respiratory infections, and otitis media. The internist wonders where the diseases he knew as a resident are, as his time is increasingly consumed by what are for him routine health examinations and boring psychosomatic diseases, i.e. diseases that are not interesting. He sees patients who live longer and who experience the frustrating diseases of aging. He has learned to treat the complications of myocardial infarctions but does not possess knowledge that tells him clearly what to do with a patient with a slightly elevated blood sugar, uric acid and cholesterol. Small wonder that present plans for health assistants include not what the assistants can do best, but what the physician does not want to do or feels uncomfortable in doing.

If medical schools continue to train physicians in the future as at present, the community role of the family physician will be performed by someone else, since the need will not disappear. It should be obvious that many patients already use others to provide them with care which is not presently obtained from the physician.

Other legitimate objections have been raised concerning this discription of the ideal. For example, can any physician give continuous care? Continuity does not mean, as has been suggested,[7] care for the same individual from the cradle to the grave. In our increasingly mobile society this is impossible. It does mean care that is continuous for the individual and his family for a given period of time. The generalist, unless he is a pediatrician or an internist, will deliver cradle to grave care in the cross-sectional sense only, in that his panel of families will contain representatives of the total age spectrum.

Continuity also means availability. The family physician cannot function alone, not just because the amount of knowledge is so overwhelming, but because no one individual in our society can any longer be continuously available. Because the physician has been available, he is more effective at time of crisis. Crisis intervention has had much theoretical appeal, but little practical evaluation. Numerous anecdotal data are available which suggest that it is a valid concept and an effective tool for the family physician. There have been no studies to demonstrate that continuity makes a difference in the outcome of health care, although some are in the process.[8] Until evidence is presented to the contrary, however, clinical experience suggests that continuity is a cornerstone of any system of comprehensive health care.

Can a physician really provide care to a family? Generalists have been assumed to deliver care to family groups, and many have succeeded. Many, inadequately trained, overwhelmed by demands of service, isolated from the hospital and medical community, have not delivered quality care either to individuals or families.

There is a body of knowledge about the family that currently is known and utilized better by other professionals than physicians, such as social workers, sociologists, educators, and psychologists. The family is the unit of health and illness because it is the unit of living.[9] However, medical education has been directed at disease processes and at care for individuals and has not really used or added to this body of knowledge with any consistency. The practicing family physician learns this very quickly. For example, the physician, if he is perceptive, is very familiar with the night call where the ill child is the healthiest family member seen and was simply the means of obtaining medical help. Streptococcal and staphylococcal infections are family disorders, and successful management requires consideration of the family group.[10]

A very real question is whether knowing families and their problems intimately can influence the outcome of illness and the maintenance of health? Again, clinical experience is helpful. What determines whether or not the child with croup is treated at home or in the hospital, may depend as much on whether or not the doctor knows the family as it does on the child's difficulty in breathing. Knowing a family can result in an illness being managed at home or over the telephone. There have been associations described between the doctor-patient relationship and the successful completion of a course of penicillin or the taking of penicillin prophylaxis.[11] It is these clues that suggest that knowing the family is important, perhaps even essential to providing the most effective medical care.

How can the physician function in the patient's home? The rapidly disappearing house call has allegedly been the victim of modern technology. It actually has been a victim of convenience. There is some evidence that the physician makes more correct diagnoses and knows his families better if he has made home visits for acute illness.[12] A house call is only an inconvenience to the physician when he has not been taught, or does not consider important, what can be learned in the patient's home.

Can a physician practice health maintenance? Prevention does not provide the same immediate satisfaction as cures. Yet, skill in applying what is known about prevention and what will be increasingly known can be the most satisfying form of practice. Unfortunately there is little evidence that early intervention in the area of mental health is effective, and there are no immunizing agents against accidents. Many diseases can be detected early, and then very little that is concrete can be done. The frustrations associated with attempting to practice preventive medicine are well known. Again, professionals other than physicians have been more successful in accomplishing prevention, perhaps because their background has not been associated with the concept of cure. Medical history is full of physicians who were ostracized by their colleagues because they attempted to institute preventive practices. It took almost 100 years for smallpox vaccination to be accepted, and antiseptic techniques were not exactly an overnight sensation. The frustrations associated with the efforts to modify diet and to have patients discontinue smoking are well known. Since we lack a methodology for practicing prevention then let the profession devote greater energy to developing that methodology.

Can the family physician function in the hospital? Statistics can be quoted that show that the patient in the hospital receives better care when he is cared for by a fulltime specialist. There are no comparable figures that suggest that the physician who cares for his patients in the hospital provides more appropriate, i.e., higher quality care for his non-hospitalized patients. These figures can and should be obtained. It could be that in the balance the scale is tipped in favor of the physician caring for his patients in the hospital, because of the better care received by ambulatory patients. Indiscriminate use of antibiotics might result from isolation from the hospital since the isolated physician may not fully appreciate safe and effective drug utilization, having been denied contact with his hospital based colleagues. It also should be obvious that the physician who knows his patient can provide needed insights, needed support, and interpret for the patient what is happening and help the patient with choices when there are choices to be made.

Another benefit of the family physician being in the hospital is that he prevents the hospital based specialist from forgetting that he, the specialist, benefits from the effective screening that has occurred before a patient is hospitalized. The family physician, because he is closest to the population at risk, can protect his patients from overtreatment and overdiagnosis. The hospital based physician should not be isolated from the community anymore than the family physician should be isolated from the hospital.

The family physician, like all physicians, has a responsibility to evaluate what he is doing. Important research must be done to see who can best fulfill the function of the family physician. It may well be that group practice with a retinue of physician assistants does represent the inevitable, and even the best way of delivering health care, but it would be better to have facts rather than feelings. Family medicine may be practiced by individual physicians, by a health team, or even by specialists whose training has included the practice of family medicine. For example, it may well be an impossible task to expect that one physician's personality is suited to providing care for patients of all ages. A family "pediatrician" may be willing to provide care for young adults but not the aged and similarly the family internist may be willing to take care of younger children but not newborns. These alternatives can be studied and compared for effectiveness, particularly as more medical schools concern themselves with evaluating systems of delivery of health care.

Not every physician is meant to do research but family physicians can organize, originate, participate in, and contribute to the body of knowledge of family medicine. The practicing physician may not be able to organize his time in the same manner as his hospital based colleagues but he is in the best position to know which questions need asking. Research for certain physicians makes functioning as a family physician an even more attractive career.

In summary, the family physician, whoever he will be, cannot practice family medicine alone. He should be a leader of a team of health professionals that will cover the spectrum of community resources. How he will do this and how he will be prepared needs careful study. It is very likely that the production of family physicians, even with a board certifying mechanism, will not in the immediate future produce sufficient physicians to meet the need for primary care. Specialists, particularly pediatricians, obstetricians, and internists, can practice family medicine and function as the family physician but can be successful only with very important changes in present specialty training. The responsibility of the medical schools and teaching hospitals is a real one. Medical students will not choose a career where they are viewed by their colleagues as second-class professionals but neither will they be first-class professionals without a demonstrated function. The responsibility of the academic community is to study this function and evaluate different models of care. There should be no doubt that the function of family medicine exists, but whether it will be provided by the medical profession and be part of the program of medical education remains to be seen.

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"Since we as judges lay no claim to expertness in these matters (the etiology of cancer) we can add nothing to the discussion, nor can we be expected to resolve these conflicts which the medical profession itself has been unable to resolve. Notwithstanding this uncertainty we think we are bound to treat the opinions of these doctors as something more than speculation and conjecture which are but polite terms for unscientific guesswork."—Supreme Court of Minnesota, National Association of Compensation Claimants. Attorneys Law Journal (NACCALJ), 8: 64, November, 1961.

Implementing the Primary Physician— Problems of Credibility and Feasibility

Richard Magraw, M.D.

Watching and participating in today's negotiations concerning the organization of medical care and health services, it is hard to escape the impression that these negotiations are close to foundering on the issue of providing "basic" "first line" or "primary" medical care and health services. Both within and outside the medical profession opinions diverge as to the importance of primary medical care and the kind of persons needed to provide it. Some feel that given the existing and forseeable number of physicians, their time and skills must be spared for more important functions than primary care. While others feel that primary care is the central medical role and that the quality of primary care is the most important single factor in determining the effectiveness of the services the American people receive. Some feel that it is impossible to truly professionalize the generalist function or the generalist. Others feel that this has already been accomplished and needs to be further refined. Some find it impossible to conceptualize a fabric of medical care which does not have as its basic social molecule, a patient or family and a highly trained physician; others do not.

These and similar differences within the medical profession incline policymakers planning medical care organization to bypass what has previously been the basic "social molecule" in the tissue of medical care organization—namely, the primary physician and the patient. Thus, in June of 1967, John Gardner, then Secretary of Health, Education, and Welfare, stated "Whether the health care system of the future should develop around the hospital as an organizational focus, or around the payment mechanism, or around group practice plans, or around all of these in some sort of collaboration with State health planning councils—or whether other variants will emerge—is still a wide open question."* It is noteworthy that Mr. Gardner did not include in his catalogue of elements which might serve as a focus for organization of medical services the primary physician, and I believe this reflects a failure to achieve a consensus about this within the medical profession.

This point is made to emphasize what has been and continues to be one of the chief blocks to the implementation of the concept of the new physician, namely, our confusion, as a profession, about the realities of our time. We have not understood the sweep of change and have consistently underestimated the complexity of the adaptations which are demanded of us.

For example, there has been a general assumption that the task of implementing the new physician could be accomplished simply by persuading the medical schools and teaching hospitals to develop an appropriate instructional program for family practice; whereas to implement the new physician not only must medical education (undergraduate and graduate) be restructured, but the division of labor within the traditional medical profession must be revised, the relationship and functions of the elements of the larger medical care apparatus; i.e., clinics, hospitals, and related health personnel must be modified, arrangements for payment for medical services will need to be significantly altered and public understanding and acceptance must be won. In each of these areas there are obstructions and pitfalls. For ease and clarity of presentation we can consider them in clusters as indicated in the sentence above.

I. *Blocks to the Implementation of the New Psysician within Medical Education.*

A. Blocks within the medical school and its associated Hospitals and Clinics.

Presented at the Michigan State Medical Society Annual Meeting, September 27, 1967, Grand Rapids, Michigan, under the title "Pitfalls in Implementing the New Physician". Most of this paper was previously published in Michigan Medicine June 1968 under the title of "Obstructions and Pitfalls in Implementing the New Physician."

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* Report of the National Conference on Medical Costs, Washington, D.C. June 27-28, 1967, p. 79.

Although most schools are currently undertaking some modification of undergraduate curricula, for purposes of this discussion we will not consider undergraduate aspects of education for this new role, since it is not absolutely essential for the implementation of the concept of the new physician that undergraduate education be modified as the first order of business. (We can dismiss this from extended consideration here but should at least comment in passing that many university Medical Centers are more or less "hung up" on this. They do not see how they can accommodate a new kind of undergraduate training without damaging their current "product".)

Most physicians have heard a good deal about the pitfalls and obstructions of implementing this program within the medical schools; consequently they will only be listed here in an abbreviated way.

When faculties come to consider establishment of programs for the "new physician" in medical schools, they find they have undertaken a very large order for the following reasons.

(1) In general medical school faculty members are out of practice in assessing the medical needs of society and in perceiving the characteristics of the practicing profession in relation to those needs. They are often so far removed from the communities; medical care needs as to be unable to make judgments regarding training required for primary care in today's world on the basis of their own first hand experience.

(2) Medical school, hospitals or clinics are usually either referral or charity institutions or both. As such, they have neither an established role in nor a tradition of providing first line comprehensive medical care. Further as they attempt to develop new and more suitable facilities for training, the expect objections from the practicing profession intruding into primary care and thus far their anticipations are proving correct.

(3) There is a new division of labor implicit in the concept of the new primary physician which runs counter to the existing departmental structure and the associated professional models which are strongly entrenched in medical school usages and concepts and politics.

It was the perception of this which led Dr. William Stewart, now the Surgeon General, several years ago to describe the need for a "third medical faculty." He perceived that medical schools already had two recognizable medical faculties—the basic science faculty increasingly developing a separate kind of academic discipline of its own and the departmentally and specialty and non-community oriented clinical faculties increasingly concerned with post graduate specialty training and with biological research. He noted the need for a faculty specifically oriented to the medical care needs of the community.

(4) Unnecessary opposition within the medical schools was generated when the campaign for the new physician developed in relation to implied or expressed threats to the research enterprise which is the overwhelmingly preponderant forces in today's medical school.

(5) The absence of designated federal funds for the graduate training of primary physicians is another problem. Although in the year 1966, for example, the National Institutes of Health and more modestly other branches of the Public Health Service had $324 million for training* in various specialty categories—i.e. cardiology, rheumatology, psychiatry, neurology, none was earmarked for training of primary physicians or family doctors.

(6) The traditional medical school has evolved into a Medical Research and Training Center. The medical educational part of this enterprise (as opposed to the research portion) is not rich enough to undertake a new training program without major additional financial support.

(7) It is very nearly impossible for any one school to undertake the major revision of either graduate or undergraduate training required by itself. Hence, a cooperative effort is required. Further it is difficult for medical educators, even as a group, to seriously undertake to produce a "new physician," including a new role, unless the institutions and arrangement of medicine and society are also changing so as to provide a place for him.

All this adds up to the fact that in addition to lacking facilities, faculties lack incentives for implementing this program. Academic medicine has a conservatism of its own which in this matter appears to be about as intransigent as that of the practicing profession.

B. Obstructions within the teaching hospitals (public or private) not affiliated with medical schools.

At the present time some of the most promising starts at implementing the new physician are occurring in these hospitals, particularly the private ones.

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* This figure is conservative as research program often are used to augment training funds within medical schools and centers.

City or county hospitals (charity hospitals) are having problems with the concept. Their major problem appears to be that the medical care provided the patients by such hospital staffs has been far from comprehensive. Regardless of the quality of the in-hospital care given, overall the care usually has been fragmentary because of the hospital ward and categorical orientation. Outpatient care has been of poor quality and concepts of community health needs have been limited to calculating bed capacity and comparing the technological sophistication of the hospital with similar institutions.

Private hospitals are in a stronger position as a locale for implementing the training for the new position because doctors on their staffs provide primary care, and paradoxically because their (the doctors) work orientation is much more toward their office and the community than to the institution. Moreover, the private hospital to a greater or less extent has a recognized position of trusteeship for the medical resources of the community, thanks to Hill-Burton regional hospital planning, etc.

The most essential *new* elements for education of the personal physician are the demonstration of (1) the managerial responsibility of the individual personal physician, and (2) the linkage between such responsibility and the cooperative enterprises of medicine as in the hospital and its medical staff. At present the private hospital-medical staff combined offers the only existing demonstration of this, although the models are far from being adequate for instruction of tomorrow's physician.

II. *Blocks within the Practicing Profession.*

The obstructions within the practicing profession are not fully separable from those within the medical schools and teaching hospitals. They derive from a tendency among some doctors yet to see this as a circumscribed issue involving fundamentally the general practitioners rather than seeing the issue as a general restructuring and rationalization of medical care or understanding the need for such restructuring and also from the unconscious resistance on the part of almost all of us to relinquishing a cherished but unfulfilled part of the professional role.

At the present time the chief overt opposition to this concept comes from some groups of internists and pediatricians and to a considerably lesser extent from the obstetricians and general surgeons. Not surprisingly the publication of the Millis and Willard reports as well as the other reports and publications which have supported the concept, has resulted in a crystallization of opposition to the concept of a "new primary physician" within the groups which feel they might be adversely affected.

Pediatricians and internists have objected to this concept because they sensed in it a contrived revival of the surgically oriented and in their view inadequately trained general practitioner, and perhaps also a role which if not a threat to or criticism of their present work and training at least required change.

In general this is perceived as a threat rather than an opportunity for the evolution of roles and editorials in some journals this past year, while acknowledging that there are now different kinds of internists and pediatricians which may require different training tend to see these as variations within the disciplines of Pediatrics and Internal Medicine rather than as replicas on a smaller scale of the generalist-specialist problem which has plagued us all in medicine.

As yet there appears not enough awareness among internists and pediatricians that in the long run not only the interests of the American public, but the self interest of all personal or family physicians regardless of professional label or type of training, will be best served by defining this function and improving it by training. As the bottom of this problem are two cherished misconceptions. First, internists and pediatricians are holding onto outdated concepts of their actual training and their real work as that of being simultaneously broadly trained "people doctors" and general consultant specialists. It is becoming clear to all that these general specialists have already been divided by their work into two broad groups—those the preponderantly provide primary care and those that serve only or primarily as consultants usually in some sub area of an entire special field. It is further becoming clear that the evolving organization of medical care demands further polarization of these roles and formalization of them. There is some similarity between the circumstances of the professional organizations of pediatrics and internal medicine at this time and that which the Academy of General Practice was in 10 or 15 years ago when it too was battling to hold on to a nostalgic model of professional function.

Second—another cherished idea is that the internist or pediatrician should be trained for the consultant aspect of his work but that he needs no special training for family or primary care. This idea can be seen behind the insistence that all internists are internists and all pediatricians are pediatricians; that is, they should all have a common training and pass a common Board examination demonstrating a consultant's level of competence. A cynic might remark that this incidentally assures that these doctors will maintain their amateur standing in the field of primary care. Of course these cherished assumptions are not limited to internists and pediatricians. In all of us, they have their root in a common identity as doctors developed as undergraduates as well as in our individual human psychological needs and grandiosities. Today's circumstance of the internist and the pediatrician is used here to exemplify an important block existing in the practicing profession generally.

Not the least of the problems of implementing this concept of the new physician within the medical profession itself is the political power and vested interest of existing specialty boards. These boards have performed good and valuable functions in society in elevating professional standards. However, it must be acknowledged that although their actions have had public effects, they have not had public accountability. Their orientations in medical care are limited by being directed toward parts of medical practice. Each specialty board has concerned itself with improved professional functions in the specialty usually by making progressively more demanding measurements of special expertise without assessing the effect of its actions on overall medical care or unmet community needs.

Taken together these forces within the medical profession seriously impede development of educational programs and recruitment for the new professional model.

III. *Blocks in the larger apparatus of medical care and health; e.g. clinics, the hospitals and related health professions.*

As noted earlier, some of the most promising beginnings in graduate training programs for the new physician are being made in private hospitals but there are some important pitfalls involved.

In what might be described as the "hospital view of medical care" the hospital rather than the primary physician, is seen as the center of gravity of medical care. This is apparent in the proposals and recommendations made by various governmental and quasi public commissions or committees concerned with meeting the medical needs of society. They recommend that hospitals* should serve as the center of care for all patients and that they should specifically manage the personal medical care and provide referral service for all persons who do not have personal physicians.

Because of the seriousness of the need, the shortage of physicians and the lack of either a consensus in or a forward looking alternative from the medical profession, this has considerable appeal, and this kind of thinking is very widespread among planners in medical care. It is one of the obstructions to implementing the new physician since it implicitly denies the need for his function. It suggests that we do not really need any professionally trained person to carry out this function, at least for those persons who have now been given medical purchasing power but do not have personal doctors. It becomes all the more important when we understand the weight which this view is likely to receive politically and recognize that hospitals heretofore have characteristically been inward looking and oriented to a concept of care of episodic disease rather than comprehensive continuing care. Thus in many ways the hospital concept of medical care is conceptually the natural antithesis to the part of comprehensive personal care which is the basic function of the new physician.

IV. *Blocks in medical economics and the payment for medical care.*

In my view the must important obstructions to implementing the concept to the new physician are in the economics of medical care and specifically in remuneration for services. Although the history of this is long and complicated, the problem itself can be simply stated. Comprehensive personal medical care has seldom been explicitly recompensed. In general it's been a "loss leader" or a "give away item" on the medical market place. Schedules of benefits of third parties are endlessly detailed and explicit in regard to technical procedures but only vaguely and implicitly if at all, do these schedules acknowledge that there is a wider element of skill and time required for comprehensive care of the patient than for obvious procedures of medicine. There is probably nothing which could be done in medical training or in the organization of medical care which would as quickly implement the concept of the new physician and correspondingly rationalize our entire system of medical care as developing a realistic remuneration for the managerial and integrating services of the primary physician. It is hard to do this on a fee basis. How can he be paid for studying the consultation report or for all the other things involved in integrating a patient's care or preventive maintenance.

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* In order to avoid false issues it is important to understand that many people use the term "hospital" here in a broadly encompassing way as the medical care apparatus of society with the physician at the core. "Medical center" or "health center" would probably be a preferable term, but the idea of hospital has both high visability and loyal constituency.

In my opinion there is no more practical way of doing this than establishing in addition to existing fees for service, some modest "retainer fee" or "availability fee" paid annually by each patient, (or on his behalf by a third party carrier) to the doctor who assumes ongoing medical responsibility for him.

Devising some way of realistically paying for comprehensive personal care would probably brush away all existing obstacles in the path of the implementation of the primary physician. It would define in the mind of the public, the professional role which has become all but invisible under current medical care and medical pay arrangements. It would similarly define in professional thinking the function which some doctors still regard as an attempt to give to "airy nothing a local habitation and a name." Payment gives it substance. In this regard it's well to recall the bitter struggles which occurred within the last few years over the issue of surgical privileges in hospitals for general practitioners. These struggles were not wholly or even primarily economic. They grew out of the general practitioner's difficulty in defining a professional role for himself or maintaining a professional identity in other terms than surgical expertise. Surgery was what he got paid for and it was correspondingly in surgical terms, that he defined his function and measured his professional identity.

The personal physician's situation regarding pay for comprehensive personal care is analagous to that of the saloon keeper and the free lunch in the days when the lunch was supplied to help sell the beer which made the profit. By analogy the beer is the technical part of medicine that third parties pay for. When the beer was separated from free lunch (that is the surgery was separated from the comprehensive personal care) not only was the doctor's livelihood affected but his professional identity was diluted and threatened.

V. *Blocks in public understanding and acceptance.*

Perhaps the biggest block to public understanding and acceptance of the new physician is a psychological one wherein the individual members of society particularly at a time when they are not sick or actively patients, maintain the fiction that illness or disease is an alien external thing which can be dealt with, removed or cast off without involving them personally.

The potential dependence on another person, the lessened interpersonal distance and the trust required all are a little frightening and will be avoided like "flouridation" unless their usefulness is understood.

At present the implementation of the primary physician may still be in professional hands but soon and in any event, ultimately this will be a social or political decision. There is at present no constituency for personal medical care in society and at the summits of power in public affairs. This lack becomes all the more obvious and its consequences more apparent when we note the existence of and effectiveness of a strong constituency in biological research as in the axis which has developed between the medical schools and NIH, or when we understand the constituency developing in Medical Economics where predominantly Blue Cross and the Social Security Administration and to a lesser extent Blue Shield, private insurance companies and other interested parties form a defined body of special interest, competence and social and political influence.

This professional role concerns all doctors, not only general practitioners, internists and pediatricians as it will bring to pass a long overdue and adaptive division of labor. Successful implementation of this new physician is of importance to all Americans as it will provide integration at the interface between the individual patient and an increasingly complex technology and apparatus of medicine.

Failure to bring this about is almost certain to cost us part of what we value the most, the human content of our lives.

The Connecticut Regional Medical Program and the Family Physician

Henry T. Clark, Jr., M.D., Edward F. Morrissey and Conrad Seipp, Ph.D.

The Connecticut Regional Medical Program, by the terms of its legislative mandate, is dedicated to the provision of the best possible patient care in the fields of heart disease, cancer, stroke, and related diseases. All of the elements of the health care system in Connecticut—the two university medical centers, the various patient care, educational and research institutions and agencies involved in the health field, and the related practitioners—collectively share in this concern. The care of patients is the common end product to which each contributes. This common denominator of concern has been the base on which the Connecticut Regional Medical Program has brought the various elements of the health system of the region together for planning purposes.

There is today a growing recognition of the need to strengthen cooperative arrangements among the elements of the medical care system in Connecticut. The reason is to insure the delivery of comprehensive, high quality medical care to the entire population of Connecticut. Comprehensive care has many dimensions. It involves first of all completeness. It seeks to integrate prevention with treatment and rehabilitation, and to foster the active promotion of health and education for it. It seeks to maximize the availability and accessibility of quality care, provided on a multi-professional basis and in a personalized manner. It also underscores the importance of continuity, both in the provision of care and in the assumption of responsibility for it.

In a region such as Connecticut which is so richly endowed with resources for the provision of medical services, the problems of improving patient care do not center primarily upon the creation of additional facilities, the introduction of new technologies, or the augmentation of the total supply of health manpower. Rather, the essential task is to meet the needs of the population at the local level in ways which insure the most effective use of the great potentials available within the region.

The mission visualized for the Connecticut Regional Medical Program is to identify, promote and assist in the organization of the optimum relationships and functional linkages among the various elements of the health care system of Connecticut. Given its emphasis upon strengthening local performance, the program faces in two directions. On the one hand, the program seeks to stimulate organized and sustained planning within the ten health service areas of the state. The aim of such planning is to foster the development of the fullest working arrangements between community hospitals, and among those hospitals and the various extended care facilities and programs, the public and voluntary health agencies and the community-based practitioners. On the other hand, the Connecticut Regional Medical Program seeks to ascertain the ways in which the two university medical centers and the other statewide resources of the Connecticut region can best make available their specialized competencies and skills as technical backstopping and reinforcement to the practitioners and institutions which render care at the local level.

The plan of action of the Connecticut Regional Medical Program is premised upon the conviction that the effectiveness of each element of the health care system in Connecticut will be enhanced by strengthening the cooperative arrangements among them. The family physician must be viewed as the foundation of a total system, and his effectiveness in the future depends to a great degree upon the quality and the scope of the relationships which are developed between him and other partners who are involved in the provision of comprehensive care to patients. Accordingly, it is necessary for the Connecticut Regional Medical Program first to identify and then to assist in mobilizing those resources which will help the family physician to discharge

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his responsibilities to his patients. The development of the optimum relationships among the various components of the health care system must start at the local level from the point of view of the community in which the patient lives, where he is first seen, and, for most of his health problems, where he is treated.

This is why the Connecticut Regional Medical Program characterizes the need to initiate and stimulate more systematic *local* planning throughout the Region as the first and most important thrust of its activity for the coming years. The Connecticut Regional Medical Program is seeking to promote the welfare of people, not organizations. It is committed to the conviction that this can best be accomplished by increasing local self-sufficiency. It follows that the purpose of strengthening cooperative arrangements is to augment local medical capabilities by insuring that the community based practitioners, the local hospitals, and the related health agencies and programs are able to obtain more readily and in an organized fashion whatever types of assistance they require to function at maximum effectiveness.

The initial assemblage of proposals which have recently been formulated by the Connecticut Regional Medical Program and submitted to Washington on March 1, 1968 as an operating grant request presents opportunities to expand capabilities of health care elements at the local level. Emphasis has been placed upon the community hospitals of the state as an essential institutional link in mobilizing the additional resources and promoting the elaboration of relationships which are viewed as necessary to insure the development of a more orderly and effective continuum of patient care at the local level. To be sure, no community hospital in Connecticut may today be completely prepared to expand the scope of its functions so as to assume the full leadership role that is required of it as an institutional base of a health care system. However, the role of the community hospital has been progressively undergoing extension in recent decades. While the hospital has not yet in fact emerged as a community health center, there is much which suggests that it will continue to move in this direction.

It is this visualization of the augmented roles of the community hospital in the future which is of particular importance in the proposal which the Connecticut Regional Medical Program has made in regard to the development of a "third faculty" of the schools of medicine. Because this proposal is also seen as of major significance in contemplating the future of the family physician in the state, it will be briefly described.

The proposal embodied in the development of a "third faculty" is aimed at assisting in the creation of more workable bridges between the health service areas and the university centers which serve as resources for the entire region. This calls, first of all, for the development of working partnerships between key hospitals and one or the other of the university medical centers. The creation of a "third faculty" of the schools of medicine through the joint appointment of full time chiefs of service in selected hospitals throughout the region is visualized as the primary vehicle for this purpose. These physicians, together with necessary supporting staff, would be based in a local hospital but would be expected to spend a part of their time in the university medical center. In turn, the clinical faculty at the university medical center would be augmented to provide counterparts to the full time hospital appointees. This would organize and synthesize the extra-mural activities of the medical centers.

This "third faculty" is visualized as assuming multiple roles. First, it will contribute to the creation of an environment in a number of community hospitals in Connecticut in which some medical and dental student instruction might be given in the future. Second, it will augment substantially the quality and scope of intern and residency training programs in many Connecticut hospitals. Third, it will serve as a major force for the organization and provision of continuing education activities for practicing physicians, dentists and other health professionals. Fourth, it will be available, through consultation, to assist in the management of selected patients. Fifth, it will participate in the analysis and evaluation of patient care in the hospital it serves and throughout the surrounding health service area. Sixth, it will provide leadership for the development of many specialized medical services in the hospital it serves and thereby, in time, produce a greater level of medical self-sufficiency at the local level. Seventh, it will expedite and facilitate the process of selected patient referral to the university medical centers. And eighth, it should become a key resource for the planning and coordination of all medical care activities in its health service area, including medical care programs for the disadvantaged segment of the population. In all of these respects, this "third faculty" will help mobilize outside medical resources, as appropriate, and will act as conduits for bringing the expertise and special capabilities of the universities and the other regional resources into medical practice at the local scene.

The future of the family physician is tied in with the future of the health care system as a whole. Both must respond to the twin forces of an accelerating accumulation of new medical knowledge and an increasing specialization of effort. Only through organization is it possible to deal with the resulting problems. In order to insure that the maximum benefit will be derived from the application of specialized medical knowledge without incurring the costs of further fragmentation, duplication, and depersonalization of the care rendered to individual patients, it is necessary to develop more effective communication and interaction between the local practitioners and the medical center. The task is to preserve and extend the integrity and traditional humanity that has been embodied in the practice of medicine and at the same time to facilitate the fullest application of scientific advance.

The development of the "third faculty" can be viewed in functional terms as one important vehicle for linking more effectively the specialized medical capabilities and resources which are to be found in the Connecticut region with the provision of care at the local level. It should be recognized that inherent in the existing division of labor are varying levels of specialization. The community based "third faculty" represents the introduction of an essentially new element into the structure of medical care organization in the region. Such persons, in their role as service coordinators, can be expected to monitor and integrate the most highly specialized aspects of the regional medical care system in terms of interests and the needs of the family or personal physician. While individual members of the "third faculty" will be oriented to practice as it relates to a single service, these individuals will act as a bridge between further specialization related to that service and the local practitioner. Because of their concern with medical practice in terms of particular institutions and communities, there will be a natural tendency for them to work as a team in providing assistance and support to all persons who are responsible for the provision of patient care in the area in which they serve.

This "third faculty" constitutes one of a number of proposals which have been made by the Connecticut Regional Medical Program for introducing new kinds of relationships and functional linkages among the various parts of the health care system. All of the proposals are seen as mechanisms for reinforcing and backstopping the local practitioner, thereby enhancing his role. Each part of the regional medical care system has its own essential functions. It is the aim of the Connecticut Regional Medical Program to strengthen through cooperative arrangements the interconnections between these various parts. Each has much to learn from the other. Success in the development of this proposal for a "third faculty" depends not only upon widespread understanding and support; it also depends upon continuing planning at the community level. Only through such involvement will it be possible to derive from this proposal its potential for facilitating the ongoing transmission of the fruits of medical specialization into the practice of comprehensive community medicine.

Silence is one of the hardest arguments to refute.—Josh Billings

THE PRESIDENT'S PAGE

It means much to be a general practitioner, a family doctor, dedicated to the art of caring for the ills of the whole family, regardless of sex or age. Who can deny there is a tremendous satisfaction in being so closely associated with patients? Much has been made of the fact that the family physician performs many services other than medical—and rightly so. He is the priest, father, and healer rolled up in one man. No man in general practice can escape being imposed on to perform such services. This, it seems to me, is one of the real joys of general practice.

The general practitioner of today is a far cry from the family doctor who practiced 25 years ago. His office is just as modern as city offices. He must spend time constantly enlarging the scope of his knowledge. It is not enough to treat patients with the same equipment, both mental and physical, year after year.

The ranks of those who practice general medicine are rapidly thinning. This has come about for several reasons. It has become popular to have various ills treated by a specialist. This almost becomes a status symbol. Many doctors have felt it unwise to cope with the vast field of medicine and have, instead, focused their attention on a small segment. The patient who elects to choose a specialist to treat a given complaint may make an error in self diagnosis, thus delaying proper treatment while he is being referred to the man he should have been consulting. The end result will certainly be the same, but the delay may be costly. The doctor who is concentrating on a small segment of medical knowledge may indeed be losing the satisfaction which comes with the more general knowledge of medicine.

We must give real thought and effort to increasing the number of men practicing general medicine. These men are in short supply. Indeed, the matter is urgent and critical. Even now many good sized towns are without adequate general medical personnel. What can be done to encourage young men to spend their first few years in general practice? Certainly it is well known that a man who has devoted time to general practice makes a better specialist because he knows the problems of the whole man.

The shortage of general physicians is a challenge to us all, but especially to the educators of future physicians. These men who are teaching our young doctors must arrive at some method to increase the number of family physicians. We in organized medicine must do all we can to help reach this goal. Together we should be able to do it.

Let us remember the deep satisfaction the family doctor gets when he drives up to a house and a voice cries out, "It's all right, Ma, Doc's here."

Norman H. Gardner, m.d.

WHEN CARE FURNISHED TO ECF PATIENTS CAN BE COVERED BY MEDICARE

The Bureau of Health Insurance, U.S. Social Security Administration, has issued a statement clarifying the level of care in an extended care facility which can be considered a covered service under Medicare. It is printed in full below as a guide to physicians.

To assure prompt and equitable determinations as to whether care furnished to patients in extended care facilities is covered and can be paid for under Medicare, the understanding and cooperation of physicians, hospitals, ECFs, utilization review committees, intermediaries, and carriers are vital. We hope this message will help to achieve these objectives.

A. WHAT IS "EXTENDED CARE"?

The covered level of care provided when the patient's condition upon his discharge from a hospital requires him to be in an institution for the primary purpose of receiving continuous skilled nursing services and other professional services.

B. WHAT ARE "SKILLED SERVICES"?

A skilled service is one which must be furnished by or under the supervision of trained medical or paramedical personnel. A service is not skilled merely because it is performed by a trained medical or paramedical person. A service which can be safely and adequately self-administered or performed by the average, non-medical person, without the direct supervision of trained medical or paramedical personnel, is a non-skilled service, without regard to who actually provides the service.

C. WHAT IS "NONCOVERED CARE"?

Any level of care less intensive than extended care. Formerly, all noncovered care was referred to as "custodial care."

D. WHAT ARE THE RESPONSIBILITIES OF THE ATTENDING PHYSICIAN AND HOSPITAL?

The attending physician customarily plans in advance for the needs of his patient including, where appropriate, transfer from a hospital into an extended care facility. The hospital can and should aid in this planning process. Following is the preferred approach:

1. While the patient is in the hospital, a medical information summary should be prepared including the physician's orders for the patient's care in the facility, a profile of the patient's condition, and the services expected to be needed.
2. This summary should be submitted by the hospital to the facility prior to the time of the transfer of the patient.
3. If the summary is to be incorporated into a form, it may be incorporated into a standard form agreed to by the intermediary and the providers of service.

When this information has not been submitted in advance as indicated above, alternate approaches should be used to supply the needed information. We have been advised by the medical profession that good patient care requires the extended care facility to have available by the time of admission, in writing, the required patient care information. The written data may in some instances be preceded by telephone orders which would make possible advance preparations for care.

E. WHAT PROCEDURES SHOULD EXTENDED CARE FACILITIES FOLLOW?

If adequate information is received, requiring it to furnish skilled services which are obviously covered care, no special action need be taken by the ECF. However, if the ECF thinks there could be reasonable doubt upon admission that the care is covered (or if, during the ECF stay, there is a significant change in the level of care), it should take these steps:

1. Complete a "medical information form" or equivalent (by the ECF's director of nursing services, the charge nurse, or a physician) based on the attending physician's orders and the transfer hospital's medical information. A copy of the hospital's medical information summary or the attending physician's orders would generally be an acceptable substitute.
2. Forward this medical information to the intermediary within 48 hours of admission or when a change in the level of care raises doubts as to coverage.
3. The utilization review committee should review promptly each admission where there is a question of whether the required level of care is covered to help screen out claims for care which are obviously noncovered.

4. To minimize the need for recontact by the intermediary, the utilization review committee should record the skilled services it considers to justify extended care on a medical information or other form, and the information should be included with any submission of utilization review committee findings by the extended care facility to the intermediary.

F. WHAT ACTIONS WILL THE INTERMEDIARY TAKE IN ITS DETERMINATIONS?

1. Process medical information forms promptly and inform the ECF of the results.

2. Where the care is deemed covered, reimburse the ECF as long as the patient requires that level of care, up to the maximum benefits.

3. Where the ECF is conscientiously carrying out the procedures listed above in each questionable case, the intermediary will presume that a case with unclear evidence is covered up to the time when the ECF is advised that additional evidence and evaluation by the utilization review committee is required. However, if the ECF has not been following the recommended procedure for questionable cases described above in (E), retroactive denial may be made back to the date of admission or any subsequent date established by the evidence.

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SENIOR PHYSICIAN—Opening for Senior Physician—$16,370-$19,970. Many liberal benefits. Live-in at minimal cost. Write Veterans Home and Hospital, Rocky Hill, Connecticut or call 529-2571, Ext. 395.

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ANESTHESIOLOGIST—to associate with another anesthesiologist at the World War II Veterans' Memorial Hospital, Meriden, Connecticut. For further information, contact Marvin Albert, M.D., World War II Veterans' Memorial Hospital, Paddock Avenue, Meriden, Connecticut 06450, or telephone 237-5531.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

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Special Article

Endocrine Effects of Psychotropic Drugs: V. Pituitary - Thyroid Axis

Richard I. Shader, M.D., Myron L. Belfer, M.D. and Alberto DiMascio, Ph.D.

Psychic state is known to be influenced by under activity or over activity of the thyroid gland. In turn, there is increasing evidence that thyroid gland function may be influenced by psychic state. Alterations of thyroid metabolism have been implicated as etiologic factors in certain types of mental illness, and in specific types thyroid gland metabolites have been used therapeutically. In this fifth article in our series, we review some of the literature on thyroid metabolism in mental illness, as well as the controversial and sparse literature on the effects on thyroid metabolism of the more commonly prescribed psychotropic drugs.

Psychological manifestations of hyperthyroidism (thyrotoxicosis, Graves's disease, Basedow's disease) are present in almost every case and include anxiety, tension, physical and autonomic over activity, and emotional lability with depression, suspiciousness, euphoria or apathy occurring less frequently. More severe mental disorders also occur[1]. Psychosis of the organic reaction type is common in severe cases with or without thyroid crisis prior to the initiation of antithyroid treatment. Delirium *per se* may be caused by the drugs themselves. Other psychotic pictures may be seen, including: manic-depressive reactions, agitated depressions, schizophrenia, and occasionally mania. The incidence of these psychoses in hyperthyroid patients is in dispute. A recent study by Bursten[2], found ten patients with psychosis and concurrent thyrotoxicosis among 8,000 patients admitted to a New York mental hospital. The conclusion drawn was that this combination was not a clinical rarity. Other studies indicate that about 20% of hyperthyroid patients develop overtly psychotic symptoms[3]. Asymptomatic individuals with elevated values of^{131} I uptake are said to show personality characteristics similar to those of patients with hyperthyroidism[1].

There is a wide agreement that psychological factors may determine the onset of hyperthyroidism, although the evidence is not incontrovertible. Gibson[4], found in a review of the work of the past forty years, that severe emotional shock may precipitate the disease in genetically predisposed individuals, but, more significantly, prolonged tensions and chronic emotional stresses appear to be more important etiologically than acute stresses. The incidence of emotional precipitants was said by Lidz[5] to average 80%.

Psychoanalytic studies have postulated that there are significant similarities in the basic needs and defensive patterns in hyperthyroid patients, most of whom are women. Ham[6], in a very thorough review of the clinical, anthropologic, phylogenetic, and physiologic aspects of thyrotoxicosis outlines a succinct, specific psychodynamic formulation that incorporates many features of other observers. The mechanism involves frustration of dependent longings and a persistent threat to security (exposure to death and other threatening experiences) in early life which brings about unsuccessful and premature attempts to identify with the objects of the dependent strivings. There is a continued effort toward premature self-sufficiency and attempts to help others. Resultant failure of such efforts then precipitates thyrotoxicosis. Case histories and various statistical data are cited in support of this hypothesis.

Paykel[7], in a study of thirty-five patients with thyrotoxicosis and an equal number of controls

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challenges the finding of a specific psychodynamic pattern. He found no differences in a comparison of predisposition to psychiatric illness, past and recent adjustment, psychologic responses or in historical factors of childhood happiness, and the incidence of emotional stress at onset. He attributes his finding to more careful observation of a control group.

The usual therapeutic approach to hyperthyroidism is to correct the metabolic disturbance by appropriate medical or surgical means. In addition, relief of anxiety and agitation may be achieved by use of sedatives or tranquilizers with knowledge of their possible effects, as will be noted. Following this, psychotherapy is sometimes employed to deal with the emotional factors that are important in the etiology of the disease, depending on the individual needs of the patient. Alternatively, some physicians[8] recommend psychiatric consultation, and in some instances treatment, prior to medical or surgical intervention. Persons psychologically maladjusted before the onset of thyroid disease may require psychiatric follow-up therapy; this is probably essential to prevent relapse and for successful long-term treatment.

Hypothyroidism with mental illness has been of interest to psychiatrists since William Gull[9] noted mental changes when describing the disease in 1873. The etiology of this condition has been discussed by many investigators but still remains unclear. The incidence of severe mental disorder in hypothyroidism increases with the severity and duration of the condition. It is generally agreed that the most frequent psychopathological symptoms found in myxedema psychosis are psychomotor retardation, depression, delusions, and auditory or visual halucinations[10]. Less frequent symptoms include memory impairment, disorientation, restlessness, irritability, fearfulness, misidentifications and perseverations. Michael and Gibbons[11], reported that excitement also occurs. Suspiciousness is also common.

There is a widespread belief that the mental symptoms caused by myxedema disappear when the patient is made euthyroid. However, investigation[12] has indicated that the psychopathology found in this condition is largely determined by the "prepsychotic" personality. Recent investigation by Tonks[13] indicated that some cases with disturbance in consciousness and a duration of illness of less than two years are those most likely to respond favorably to the administration of thyroid. The remaining cases are less likely to show a lasting response to hormone replacement therapy and are best managed like psychoses of unknown etiology, that is, with psychotropic drugs and psychotherapy. Glucksman[10], presents an interesting case illustrative of these treatment principles. It is considered unlikely that emotional factors are important in the production of myxedema.

Many influences on thyroid function have been documented, but the results are generally inconsistent. The effect of traumatic stress on thyroid function has been fairly extensively studied in experimental animals. Prolonged increases in thyroid activity in rats were demonstrated following stress by Leblond and Hoff[14], though other workers using rats and other animals found opposite effects. Starvation[15], radiation[16], burns[17], tourniquet shock[18], restraint[19], formalin injections[20], and other "emotional stresses"[21] have been shown to depress thyroid function. The accumulated evidence suggests that it is unwise to apply these findings directly to man. Reiss, Forsham, and Thorn[22], state that in human subjects there was an increase in uptake of ^{131} I by the thyroid gland following adrenaline injection. Other work[33] by this same group showed that an injection of ACTH and cortisone produces a depression of the ^{131} I accumulation gradient and of serum protein bound iodine (PBI) although exogenous thyroid stimulating hormone (TSH) was still capable of producing an increase in thyroid secretion. A marked and sudden increase in urinary excretion of iodine following operations was demonstrated by Perry and Gemmell[23], although they were unable to demonstrate any change in the level of serum PBI in 11 patients. This suggests that the metabolism of iodine and possibly that of thyroxine was altered following trauma. This work was confirmed by others[24 25].

Engstrom and Markardt[26], measured the level of serum PBI for five days following surgical operations but no definite changes in the overall levels were noted, except in three dying patients who had very low serum PBI levels. Although the overall level of circulating PBI appears to remain constant, this does not necessarily mean that the thyroid is unaffected by stress. A series of papers by Goldenberg and co-workers[25 27 28], suggest there are changes in thyroid activity during stress. It is possible that changes in rates of production, utilization, and excretion occur, even though blood levels of PBI remain constant. Volpe, *et al.*[29], failed to show an effect on the normal thyroid gland of severe mental and physical stresses or strains. A most interesting observation has been recently made by Mason[30], that emotional factors can increase thyroid function. He found that prolonged aversive conditioning raises the plasma concentration of thyroid hormone in the monkey. Alexander, *et al.*[31], in a study comparing the psychological and hormonal responses of acute hyperthyroids, treated hyperthyroid patients, and controls to a psychological stress showed a significant rise in radioactive labeled PBI levels in all hyperthyroids, but all treated hyperthyroids showed a sharper and more rapid decline following cessation of the stress. Controls showed a depression followed by a slight rise. The use of counterphobic defenses was more common in these hyperthyroid patients than in the controls. Mason, *et al.* [32], recently found, along with other hormone changes, a decrease in PBI before the onset of upper respiratory infection—tentatively hypothesized to represent a response to stress. In many of the studies involving stress the participation, and perhaps inhibition of thyroid function by increased levels of 17 OHCS or ACTH have been postulated as significant. It has been shown that administration of large doses of ACTH or cortisone will reduce the basal metabolic rate, serum PBI, and thyroidal ^{131} I uptake[29 33-37].

Fessel[38], has shown a rise in 4S and 19S serum proteins as a result of severe mental stress. In reviewing the literature, he notes that mental stress and disturbances of the diencephalon and hypothalamus have been found to affect markedly blood proteins and the general immunological mechanism. Thyroglobulin is a 19S protein. Perhaps some of the data on thyroid elevation following stress may primarily represent more general protein alterations.

Prange[39], discussing the role of norepinephrine in depression makes two observations: 1) Hyperthyroid patients are exquisitely sensitive to the effects of both epinephrine and norepinephrine, while hypothyroid patients are relatively insensitive. 2) Depressed patients have been thought to have disordered thyroid functioning. This observation might now be explained by the catecholamine alterations in affective disorders. Catecholamines are also altered in anxiety-tension states.

Friedell[40], reported that patients who were in a chronically tense state had elevated levels of ^{131} I uptake by the thyroid gland. He demonstrated in a double-blind, placebo controlled study using meprobamate with and without benactyzine, that when the tension, excitement or nervousness of his patients subsided with drug treatment, the ^{131} I levels returned to normal. Thus, the levels of anxiety and tension in patients undergoing treatment with psychotropic drugs must be considered in the evaluation of drug effects on thyroid functioning. This was further supported by work of Durell, Libow, Kellam, and Shader[41], who found that thyroid activity correlated significantly with degree of psychosis in patients with periodic psychotic episodes. PBI levels were found to be significantly increased in association with the onset of psychotic decompensation and ^{131} I uptake was found to be elevated during the onset of psychosis, It is important to emphasize that these changes are measured using the patient as his own control. The patients studied almost always had levels which were consistent with a euthyroid state. Also of importance, may be such factors as diagnosis, chronicity and diet. For example, Bowman and co-workers[42], found significant differences between the serum PBI values of paranoid schizophrenic patients and schizophrenics of other subtypes. Simpson, Cranswick and Blair[43], studied 28 patients with chronic schizophrenia, and found clinical signs of hypothyroidism in 28% and decreased ^{131} I uptake in 93% of cases, although serum PBI levels were within normal limits. Values for ^{131} I uptake for newly admitted first-admission schizophrenic patients were intermediate between those from the chronic schizophrenics and a group of normal controls. These findings were extended and replicated in a subsequent study[44]. In addition to diagnosis and chronicity, diet and nutritional status may alter thyroid function. For example, increased T_3 uptake, decreased thyroxine-binding globulin (TBG) and thyroxine-binding prealbumin (TBPA), and increased serum-free thyroxine have been reported in fasted obese patients[45]. Thus, decreased caloric intake in depressed or catatonic individuals, for example, might be a relevant factor in the assessment of the effect of psychotropic drugs on thyroid function.

Studies have also been carried out on the effects of psychotropic drugs on thyroid function in non-psychiatric patients. Földes[46], studied the short term effects of chlorpromazine on PBI in six euthyroid, non-psychiatric subjects. Following baseline studies, 50 mg I.M. of chlorpromazine was given and it was found in five of the six cases that there was no effect on PBI. This is in contrast to Lövie[47], who demonstrated a rise in the PBI level following prolonged chlorpromazine treatment. The duration of treatment appears to be one of the more critical factors, as will be seen subsequently. Newman and Fish[48], in a series of 31 euthyroid and 12 hyperthyroid patients indicate that the administration of promazine, meprobamate, hydroxyzine, or reserpine in the usual therapeutic doses for a period of 10 to 21 days does not alter the thyroidal ^{131} I uptake or the serum levels of cholesterol and PBI in euthyroid or hyperthyroid patients. Similarly, Lövie[47], and Földes[46], with chlorpromazine, failed to find any thyroid effect in hyperthyroid patients. Both found an intensified tachycardia in hyperthyroid patients treated with chlorpromazine and do not recommend its use in hyperthyroid patients for this reason. However, chlorpromazine in combination with hypothermia has been shown[49] to reduce signs of thyrotoxicosis. Hypothermic coma was reported in two myxedematous patients receiving chlorpromazine[50].

Contrary to the previously cited work of Bowman[42], and Cranswick[43], it has been shown by several investigators that the schizophrenic process does not affect the BMR, PBI, or ^{131} I uptake, [51-59] except in the special case of periodic catatonia euthyroid schizophrenic patients with a median hospital residence of 12.5 and years maintained on daily doses of 100-400 mg of chlorpromazine showed no change in ^{131} I uptake, PBI, serum cholesterol or BMR when imipramine, isocarboxazid, trifluoperazine, or dexedrine in usual therapeutic doses were added to the regimen. Cramer and Pover[60], also showed no particular stimulant effect of chlorpromazine on thyroid function in daily doses considered therapeutically effective—again, the men were in the hospital at least 10 years and ages ranged from 30 to 60 years.

Fink, *et al.*[61], and Blumberg[62], both from the same laboratory, have reported that ^{131} I uptake was increased in subjects receiving chlorpromazine. Further, it was noted by Fink, *et al.*[61], that the "findings were prominent in the total group of subjects, and in analysis by diagnosis in the schizophrenic group, and insignificant in the depressive subjects." Unfortunately, no details as to population, measurement, or correlations are given. These questions are significant in that chlorpromazine was given in a dose range of 300-1200 mg with proportionate doses of procyclidine, in both studies. The upper doses are above those used by the other investigators previously noted. The role of procyclidine requires further investigation. Blumberg[62], in a small group of placebo plus procyclidine subjects, found no alteration in ^{131} I uptake, but a synergistic effect between procyclidine and chlorpromazine cannot be ruled out. In light of normal variations in thyroid function, the arbitrary cutoff a 5% rise in ^{131} I uptake as being significant can also be questioned. Reichlin, *et al.*[63], treated ten male psychotic patients (unresponsive to conventional treatment) by sleep therapy with a drug combination that included chlorpromazine (600-2000 mg/day), phenobarbital (240 to 360 mg/day), sodium pentobarbital (300 to 1160 mg/day) and promethazine (100 mg/day if needed). A highly significant difference in thyroxine turnover was noted in the last 10 days of treatment, while no significant difference in the PBI levels was found. Many variables enter into such a study, and can potentially influence the turnover rate. Reichlin notes the possible effects of the multiple drugs used as both effecting tissue utilization and thyroxine binding proteins. The uncoupling of oxidative phosphorylation is noted with both barbiturates and chlorpromazine. Also drug-induced sleep conceivably could raise the thyroxine turnover rate by lowering the level of plasma thyroxine binding proteins. Chlorpromazine administered alone in a dosage up to 600 mg/day to five ambulatory patients showed no significant change in turnover rate; all patients had a lower PBI level while receiving the drug than when not receiving it, but all values were within normal range. This study by Reichlin, as well as those of Fink and Blumberg, clearly point to a need to consider dosage and duration phenomena.

An interesting finding has been the documentation of variable iodine uptake by the thyroid of the same individual when serial determinations with ^{131} I or ^{132} I are made[64]. Hare and Haigh[65], observing the same phenomena in both normals and psychotics, attempted to define the variation and were left with the suspicion that such a rise might sometimes be due to a period of heightened alertness. Cramer and Pover[60], in their cyclical patient, and Durrell and co-workers[41], document supporting findings. Cramer and Pover[60], postulate that in man the thyroid may be responsive to significant external events, whereas it is unaffected by those internal events which manifest themselves as psychiatric syndromes (e.g., anxiety states, manic excitement, stupor, active paranoid schizophrenia, etc.). In light of the current research on the responsivity of the limbic system, this argument may be spurious. The documentation of normal variability must be borne in mind when assessing reported correlations. It is noteworthy that the only place where thyroxine and tri-iodothyronine have been efficacious as therapeutic agents[66] is in periodic catatonic schizophrenia—an infrequently diagnosed syndrome.

Perphenazine was only briefly mentioned above, but it deserves special attention. Cranswick, Simpson and Nies[67], found that perphenazine produced elevated serum PBI values in 11 of 32 patients. This finding was confirmed by Oltman and Friedman[68], but was not confirmed by Ayd[69], or Hollister and Bennett[70]. It has since been suggested that this perphenazine effect was more marked for those patients who received perphenazine manufactured in 1962[70 71]. Iodine was found in the perphenazine[72], however, the authors mention that the biological half-life of the iodine compound would have to be longer than could be reasonably expected in order to account for the persistent elevation in some patients two years later. Hansen and Siersbaek-Neilsen[71], in a recent study, have found less marked increases in PBI in newly treated cases as compared to their own results from 1962. They conclude that it is likely that perphenazine tablets contain an iodine compound which in some subjects may become bound to a serum protein fraction.

Hollister and Bennett[70], found no effects on thyroid function from a combination of perphenazine and amitriptyline. Bennett and Hamilton[59], found no effect with the combination of imipramine and chlorpromazine, or isocarboxazid and chlorpromazine. Blumberg[62], in the study reported above, found no significant changes in ^{131} I uptake with imipramine alone, in doses of 75-300 mg. Fink[61], alludes to a change in ^{131} I with imipramine, but gives no details. Bailey, *et al.*[73], note the poor response to MAO inhibitors in depressed patients also receiving thyroid extract.

Oberman and co-workers[74], found no effects on thyroid function in 17 patients and normal volunteers receiving chlordiazepoxide. Baron[73], noted in patients exhibiting clinical signs of thyrotoxicosis and taking chlordiazepoxide that the T_3 uptake values were in the normal (or low normal) range, and the ^{131} I tracer test showed depressed thyroid function uptake. The significance of the latter finding is that it cannot be explained simply on interference of dissociation of protein bound thyroxine into free thyroxine, therefore, indicating that chlordiazepoxide may act as an antithyroid drug—an effect noted in animals. Harvey[76], confirms the work of baron and notes a similar effect with diazepam. Marzollo[77], also alludes to this same effect. It is, therefore, important when evaluating patients suspected of thyrotoxicosis on either of these drugs that a normal result does not exclude hyperthyroidism. Cahn[78], reported no effect from diazepam on PBI levels in normal (euthyroid) male and female volunteers.

Shader[79], studying the effects of placebo, haloperidol and thiordiazine on T_3 uptake in acute schizophrenic patients failed to find any difference among the three treatments. Of interest was the lability of thyroid function in certain patients in the pretreatment week, although values remained in the euthyroid range. It was also observed in one patient who became jaundiced, that elevated serum bilirubin produces false elevations in T_3 uptake.

Animal studies reveals a decrease in uptake of iodine after chlorpromazine[46 80-83], or imipramine[80]. Sulman and Winnik[83], reported only slight depression of thyroid stimulating hormone in rats as measured by a slight diminution in thyroid gland weight in animals receiving chlorpromazine. Marinoni[81], found chlorpromazine as effective as propylthiouracil in decreasing the uptake of labeled iodine, decreasing PBI and increasing the thyrotropic activity of the pituitary, while Aleshin[84], reported that chlorpromazine decreased pituitary thyrotropin in normal rats but increase it in methylthiouracil treated rats to a level greater than that after methylthiouracil alone. Chlorpromazine did not prevent the thyroid hyperplasia induced by thiouracil[85].

Mice made hyperthyroid by thyroid feeding were more sensitive than normal mice to the toxic effects of imipramine; they exhibited paroxysmal tachycardia and increased activity after imipramine. Hypothyroid mice were more tolerant of imipramine than were controls[86 87]. Direct inference for humans cannot be assumed but certainly caution would be suggested by the above data in the use of imipramine in other than euthyroid patients. However, Prange[88], has reported the case of a 65 year-old woman on a combined imipramine-thyroid regimen who developed paroxysmal auricular tachycardia without a prior history of cardiac irregularity. This effect was reversed when medication was stopped.

Documented cases of thyroid disease resulting from the use of psychotropic drugs have not appeared in the literature. However, the use of psychotropic drugs in patients who are hypothyroid or hyperthyroid must be undertaken with caution, as evidenced by the finding of hypothermic coma in myxedematous patients and intensified tachycardia in hyperthyroid patients treated with chlorpromazine. When evaluating the patient with suspected thyroid disease, the potential masking effects of benzodiazepams must be borne in mind. Caution should also be exercised in the use of tricyclic antidepressants in patients receiving thyroid medication and in hyperthyroid patients.

The causal relationship between emotion and thyroid illness, and psychosis and thyroid function are not proven although the data in the former are quite suggestive. The intriguing question of the mediating mechanisms in the interaction between psychological stress and observed changes in thyroid function remain unanswered, and represent a potential field for the investigative use of psychotropic drugs.

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Precautions—Pargyline: Use cautiously at reduced dosage: caffeine, alcohol, antihistamines, barbiturates, chloral hydrate, other hypnotics, sedatives, tranquilizers, narcotics. Periodically do urinalyses, blood counts, liver function tests, etc. Use with caution in liver disease. Watch for orthostatic hypotension, especially in impaired circulation (e.g., angina pectoris, coronary artery disease, cerebral arteriosclerosis); also, augmented hypotension in concomitant febrile illnesses. Reduce or discontinue if hypotension is severe. In impaired renal function watch for cumulative drug effects, elevated BUN and other evidence of progressive renal failure; withdraw drug if these persist. In surgery increased central depressant response (hypotension and increased sedative effect) can be controlled by (1) discontinuing at least two weeks prior; (2) in emergency surgery lowering dose of premedication; (3) when necessary, administering a vasopressor. Do not use in hyperactive and hyperexcitable patients. Pargyline may unmask severe psychotic symptoms where emotional problems pre-exist. Use cautiously in Parkinsonism, especially with antiparkinsonian agents. In prolonged therapy, examine for change in color perception, visual fields, fundi and visual acuity. Also, prolonged therapy has made certain patients refractory to nerve blocking effects of local anesthetics.

Methyclothiazide: Use cautiously in severe renal dysfunction, impaired hepatic function or progressive liver disease; also in pregnancy (bone marrow depression, thrombocytopenia, and altered carbohydrate metabolism have been reported in certain newborn). In surgery thiazide may reduce vasopressor response and increase tubocurarine response. Antihypertensive response may be enhanced following sympathectomy. Watch for electrolyte imbalance (e.g., hyponatremia). Give supplemental chloride if hypochloremic alkalosis occurs and supplemental potassium if hypokalemia occurs (especially in digitalized patients). Thiazides may decrease serum P.B.I. without signs of thyroid disturbance.

Adverse Reactions — Pargyline: Orthostatic hypotension and associated symptoms, mild constipation, fluid retention, edema, dry mouth, sweating, increased appetite, arthralgia, nausea, vomiting, headache, insomnia, difficult in micturition, nightmares, impotence, delayed ejaculation, rash, purpura, weight gain, hyperexcitability, increased neuromuscular activity and other extrapyramidal symptoms. Drug fever is extremely rare. Reduction in blood sugar and hypoglycemic effects are possible. Congestive heart failure has been reported in a few patients with reduced cardiac reserve.

Methyclothiazide: Blood dyscrasias (thrombocytopenia with purpura, agranulocytosis, aplastic anemia); elevation of BUN, blood sugar or serum uric acid (gout may be induced); anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice and pancreatitis. Cutaneous vasculitis in elderly patients has been reported with other thiazides.

If side effects are severe or persist, reduce dosage or withdraw drug. 804438R

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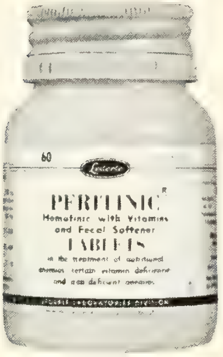

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Financing Health Care : Medicaid in Connecticut

Bernard Shapiro, Commissioner
and
Orvan W. Hess, M.D., Medical Director
Connecticut State Welfare Department

Introduction

In recent years several programs have been adopted which provide people with the means to take advantage of existing health services and facilities. This communication reviews the current status of the implementation of one of these methods of financing medical care for a certain segment of our population. Specifically, we refer to those persons eligible for medical assistance under provisions of Title XIX (Medicaid) in Connecticut. Comment is also made on the relationship of this somewhat limited resource within the total framework of medical care resource to ongoing programs of comprehensive planning for health care in this State, since financing and organization are intimately related.

Development of Medicaid in Connecticut

Connecticut's Medicaid Program was developed on the basis of recognized needs of people. It represents the result of thoughtful planning and dedication by persons who have the responsibility for the welfare and health of those who need financial assistance to meet their medical expenses.

With the adoption of P.L. 89-97 and the passage of P.A. 357 by the General Assembly of the State of Connecticut 24 June 1965, the Commissioner of Welfare was authorized to put into effect the Medical Assistance Program as provided under Title XIX, Social Security Amendments of 1965. The Governor designated the State Welfare Department as the agency to administer the State Medical Assistance Program. Its implementation would not have been successfully accomplished without the close cooperation of the State Health Department, professional groups and interested citizens. The coordinated efforts of the Health and Welfare Departments to fulfill the purpose of Title XIX, i.e., to make available high-quality medical care to selected persons unable to pay for it, is evident in many ways. Several joint committees, with shared responsibility, have been established. Agreements have been developed with the Crippled Children Section, the Office of Tuberculosis Control, the Office of Mental Retardation, State Health Department, and others to assure maximum availability and utilization services for beneficiaries.

A Medical Advisory Council, as provided under Federal Law, has been appointed by the Commissioner. This consists of twenty-eight members including ten physicians, the Deans of both Medical Schools, the Commissioner of Health, the Commissioner of Mental Health and the Commissioner of Human Rights. In addition, there are representatives of the Allied Health Professions, AFL-CIO, Ambulance Association, Pharmaceutical Association, State Dental Association, State Medical Society, Podiatry, the National Council of Senior Citizens and representatives of the poor. The function of this Committee, in which the State Health Department is an active participant, is not only to make recommendations on standards, quality and costs of medical services, personnel and facilities but to help identify unmet needs and to assist in long-range planning, evaluation and utilization. It advises on administrative and financial matters and interprets the program and its goals to professional and consumer groups.

New Directions for Medicaid

A significant accomplishment, through the efforts of this multi-oriented group, was the passage of P.A. No. 548 by the State Legislature authorizing the payment to physicians for services rendered to welfare beneficiaries on the basis of usual and customary charges at reasonable rates prevailing in their communities. Dentists and other practitioners were granted a substantially up-graded fee schedule to begin October 1, 1967.

The continuation of the usual and customary principle, governing charges for physicians, will be

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Paper presented at Connecticut Conference of Social Welfare, Southbury Training School, 15 May 1968 and 91st Annual Convention of Connecticut Pharmaceutical Association, Moodus, Connecticut 24 June 1968.

under re-consideration by the Legislature after a period of one year ending March 1, 1969. During this trial period, excessive charges and over-utilization will be closely watched. A Medical Advisory Committee, mandated by the State law, has been appointed by the Commissioner of Welfare with the State Medical Society. This consists of twenty-five M.D.'s including seventeen practicing physician members of the State Medical Society, Deans of both Medical Schools, representatives of all specialties distributed throughout all counties and three Commissioners. This group will function primarily to settle disputes regarding fees, check quality-care and over-utilization. Excellent cooperation exists with the State Medical Society which is giving its expert advice and assistance to make the Medicaid Program effective within our state.

It is felt that the usual and customary charge principle is a distinct step forward which permits freedom of choice of physician, make available high-quality care and, while preserving the dignity of the individual, eliminates the concept of "2nd class citizen medical care." It is expected that this type of remuneration may increase the willingness of doctors to provide care for these patients within their offices and lessen the load on overburdened emergency rooms and out-patient clinics at community hospitals.

It is hoped that patients will seek medical care earlier and thus possibly avoid complications which may add not only to their suffering and disability, but increase the over-all expense for subsequent treatment and health care.

Scope of Medicaid

The State Welfare Department is responsible for the administration of the Program for Medical Assistance to the following groups:

1. Beneficiaries of money payments under the Old Age Assistance, Aid to the Blind, Aid to the Disabled, and Aid to Families with Dependent Children programs.
2. Children committed to the State Welfare Commissioner under the Child Welfare Program.
3. Children under 21 who are members of a family receiving basic maintenance under the General Assistance programs.
4. Medically needy persons who are categorically related, i.e., persons who meet all the eligibility requirements of OAA, AB, AD or AFDC, except that income and resources are sufficient to meet basic maintenance needs.
5. Medically needy children under 21 not included in any welfare maintenance program. This includes the following groups:
   (a) Medically needy children under 21 years of age who are members of an AFDC family but ineligible for AFDC maintenance.
   (b) Medically needy children under 21 receiving Protective Services, Protective Supervision, Services under the Unmarried Mother's Program or who are non-committed children under the Child Welfare Program.
   (c) Medically needy children under 21 who are under the guardianship or custody of a private agency and for whom the private agency is assuming financial responsibility in whole or in part.
   (d) Other medically needy children under 21 years of age in the Community.

Extension to Chronic Illness

In February 1967, the program was extended to needy patients 65 years of age and over in mental and tuberculosis institutions. Approximately, 1,300 patients have been found eligible for the program and the cost of care is being paid by the Welfare Department. This has, however, resulted in an increased income via Federal matching funds at the level of 50% of Welfare expenditures. This current estimate is that the annual Federal revenue derived from this source will amount to $3,500,000. net.

Modification of Income Limits

The annual income limits were increased as of July 1, 1967 so that a family of four with a gross annual income of $4,400 a year is eligible to have its medical costs paid by the Welfare Department through Title XIX. Previously, $3,800 a year was the income level for eligibility for a family of four. The specific income is an increase from $300 to $600 a year for each dependent over and above the initial two persons. The personal property limits were raised from $900 to $1,400 for one person; $1,400 to $1,900 for two persons; and $100 to $200 for each additional dependent. It is estimated that approximately 15,000 additional cases will become eligible for payment of needed medical services in the course of a year.

Scope of Services Available

The scope of medical coverage in this State is comprehensive and, even at present, meets nearly all the services which must be included by 1975 under Federal standards if the State is to qualify for 50% Federal reimbursement.

Medicaid offers relief for the medical needs of the disadvantaged. It is designed to alleviate those social and health problems of the ghetto influenced by the chains of disease, disability and displacement from the mainstream of productive life. It provides the means, in accordance with recent legislation, by which the costs are shared from public funds rather than by charity or inclusion in charges for services to patients able to pay.

Program Impact Within the State

Of the nearly three million citizens in Connecticut, about 300,000 (10%) have incomes at or below the public assistance level. In July 1967, there were 1,888,200 under 21 years of age; 281,700 were over 65. Of the more than 100,000 (3%) with established eligibility for all programs including Medicaid, 70% were Negro or Puerto Rican on ADC. An average of 44,000 were receiving medical vendor payments. Thirty of forty percent of residents of ghetto areas are now Welfare and Medicaid recipients and another thirty to forty percent may be potentially eligible. During the year ending September 30, 1967, there was an increase of 7,108 cases. In this group, those eligible because of disability, numbered 1,145, while families with children under 21 accounted for 2,436. During eleven months of fiscal 1968 a total of 7,149 more cases (approximately 19,000 persons) were eligible for medical benefits than during a comparable eleven-month period in fiscal 1967. This increase in caseload, as well as other factors, has resulted in a significant escalation in the cost of health care under the Medical Assistance Program.

Type of Medical Services Secured

During 1966-67, medical vendor payments totalled $32,410,039. Payments to physicians during this period, prior to adoption of "usual and customary" principle, amounted to slightly over $2,000,000. (6.7%). More than three-fifths of the medical vendor payments were made for the care of persons in convalescent or chronic disease facilities—$20,000,000. An additional one-fifth of the payments, $6,000,000 were for hospital care although Medicare paid for much of the hospitalization for persons 65 years of age or older. These totalled nearly $26,000,000 (78.1%). The next largest expenditure was for drugs, $3,000,000, about one-tenth of the total. All other expenditures for medical services were slightly more than one-tenth of the total. The extent of added expense due to increase in caseload and utilization of facilities and services in the future is difficult to predict at this time. However, it is anticipated that, along with payment of "usual and customary" charges to physicians beginning 1st of March and upgraded fees to the allied health services, the continuously increasing public demand for health care will result in a substantially higher cost in 1968. During the first six months of fiscal '67-'68, there was an increase of about $6,000,000 in total payments for all medical services, drugs, appliances and hospitalization.

Social and Financial Implications

Recent estimates indicate that the gross budget deficit of the State Welfare Department may reach an excess of $50,000,000. About $25,000,000 of this is related to costs of the Medical Assistance Program, half of which, of course, is Federally reimbursable.[1]

Much of the increase in the Medicaid Program is due to accelerating costs in hospital and nursing home care and increased payments for general health services, such as physicians' services, dental care, and allied health services as approved by the Legislature. Hospital costs have increased during last year by seventeen percent and will be even higher the second year. Nursing home costs have risen by at least ten percent and this fiscal year will account for close to $26,000,000 of the agency's $43,000,000 appropriated by the Legislature for all medical services.

The State Welfare Department cannot alone do a great deal to control the rising costs of medical services. It is responsible for financing of a relatively small segment of total health services in the State population. However, techniques are employed for efficient administration and monitoring of utilization in order to effect a great saving, e.g., drug controls, drug bid-system, control of dental and ambulance services, length of stay in hospitals, etc.

Statistical studies have been done to determine the number of essential days of hospitalization required for most illnesses and surgical procedures. Such information may be useful for utilization review committees and of value to Blue Cross and the State Department of Health. Most of the Medicaid funds are expended for care in Nursing Homes. Doctors, caseworkers, nurses, and administrators—as members of the health care team—all can play a great role in making sure that the various types of facilities are most efficiently and wisely used and we encourage all health vendors to do so.

Social Policy Trends

At a time when the escalating costs of medical care are of general concern and a subject of Senate hearings, economic aspects may seem to outweigh purely health, humanitarian or social considerations. Yet, ill-health of our citizens is one of the greatest hazards to our national economy. In this sense, the financing of health care for the medically indigent is crucial and an expense which the State and Society can ill afford to neglect. Nevertheless, it is our responsibility to continuously take a careful look at the costs, determine whether they are reasonable and institute methods for the protection of both provider and consumer.

Medicaid and Medicare are, by law, concentrating on support for health care of those segments of Society which are in greatest need financially or burdened with the problem of dependency resulting from damaging effects of the aging process, child-birth defects, and many other types of disability. Yet, all groups and levels in our Society are so integrated and dependent on each other that, to ensure maximum productivity and economic stability of the Nation, measures must be promoted to maintain the health and well-being of *all* citizens. It is gratifying that Title XIX allows some degree of flexibility which permits a state to tailor its Program to the particular needs of its residents. In Connecticut, several new approaches are in progress as we attempt to fit Medicaid into a properly balanced relationship with other methods of financing currently used to help people meet their medical expenses regardless of economic status. If we are to achieve goals of providing high-quality care at reasonable cost, we must continue to seek out and implement innovations which will improve the organization and efficiency of administration of the system of delivery of health care services and utilization of facilities. In this concerted effort, the Regional Medical Program and the State Comprehensive Health Planning Program can be very effective. Although these programs are new and in many ways just beginning their action programs, both offer unusual opportunities for Connecticut. On the one hand, the Regional Medical Program offers the potential of improved patient care through a coordinated hospital and medical care system linking the university medical centers to community institutions and health practitioners. Hopefully, this will permit quicker application of the benefits of bio-medical research findings and technological advances to patient care and knit our medical resources together in moving towards the provision of comprehensive health care within an economic framework that is reasonable.

The Comprehensive Health Planning effort focuses on promotion of the full spectrum of factors affecting the health of the public. It presents opportunities for both state-level and local community coordination. This requires an integration of our curative, preventative and environmental health efforts through professional and consumer participation.

It is important that all who deal with health affairs recognize the significance of these Programs, their potential for progress, and challenge they present. Connecticut has an opportunity to take leadership and set a nationwide example. Educators, social workers, nurses, administrators, consumers and, especially, physicians are encouraged to become actively involved in giving their guidance to the movement towards enhancing the effectiveness, efficiency and economy of our health care system.

Reference

1. The Hospital Cost Commission established increased rates effective 1 July 1968 for hospitals, nursing homes and laboratory procedures.

OBITUARY

H. Gildersleeve Jarvis, M.D.
1885-1968

H. Gildersleeve Jarvis, M.D. died of heart disease at age eighty-three at his home in West Hartford, Connecticut after an illness of several months. He had lived an active life in retirement for the past sixteen years.

He received his A.B. degree from Yale in 1906 and M.D. from Johns Hopkins in 1910 where his early association with Walter Dandy, the pioneer neuro-surgeon began. After serving internship in Baltimore, New York and at Hartford Hospital he established his practice in Hartford in 1912.

During World War I he served as First Lieutenant in the Army Medical Corps and was a member of a neurosurgical unit in France.

Gilder Jarvis was well known for many years to the older generation of Connecticut physicians, as a prominent and leading Hartford surgeon. He was a member and past president of the Connecticut State Medical Society, Hartford County Medical Association and the Hartford Medical Society, as well as the medical and surgical staff of the Hartford Hospital. In addition he served as a corporator of Hartford Hospital for more than twenty-five years, and a member of the American College of Surgeons, the New England Surgical Society, and the founders group of the American Board of Surgery. He was a director of the Connecticut Plan for Hospital Care, and a former director of Connecticut Hospital Service, and a member of the Horace Wells Club. He served for three years as President of the Jeremiah Wadsworth Chapter of the Sons of the American Revolution.

He was also a member of the Board of Directors of the Standard Fire Insurance Company, and served for many years on the Board of Directors of the Institute of Living in Hartford. Dr. Jarvis was a member of the 20th Century Club, the Hartford Club, the Twilight Club, the Yale Club of Hartford, the Yale Club of New York City, the Johns Hopkins Surgical Club of Baltimore, the Hartford Golf Club, and was a former President of the Yale Alumni Association of Hartford.

Gilder took his name from Henry Gildersleeve, of the early colonial Gildersleeve family from which he was descended, and was born in the village of Gildersleeve of the town of Portland. Dr. Jarvis took great pride in his pre-revolutionary war ancestry, the early colonists and ship-builders of Gildersleeve.

Besides being remembered for his long and active life as a leader in Connecticut medicine he cherished the ideals embodied in being a Connecticut Yankee.

He leaves his wife Mrs. Dorothy Robbins Jarvis; a sister, Mrs. Hungerford; a son, Henry G. Jarvis, Jr.; and a granddaughter, Elizabeth Robbins Jarvis.

Louis F. Middlebrook, Jr., M.D.

In Memoriam

Booe, J. Grady, Bridgeport, Virginia Medical College, 1919. Dr Booe had been a specialist in proctology, having practiced in the Bridgeport area for over 40 years. He had served in World War I and was associated with the Bridgeport, St. Vincent's, Norwalk, and Stamford Hospitals. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, the American Proctologic Association, and the New England Proctologic Association. Dr. Booe died June 16, at the age of 75.

Garcin, Cecil R.—Danielson, McGill University, 1926. Dr. Garcin was a physician and surgeon at the Day-Kimball Hospital, Putnam, for many years. He was a veteran of World War II, having served with the Navy. He was a member of the Connecticut State Medical Society and the American Medical Society. He was a fellow of the American College of Surgeons. Dr. Garcin died June 24, at the age of 68.

Heafey, John R., East Norwalk; Syracuse Medical School, 1934. Dr. Heafey had been a pediatrician in the East Norwalk area for over twenty years. He was attending physician at Norwalk Hospital. He was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Heafey died July 6, at the age of 61.

LaPalme, Leo G.—Mechanicsville, Tufts University School of Medicine, 1944. Dr. LaPalme had been practicing medicine for approximately 20 years and had been on the staff at the Day-Kimball Hospital. He was a member of the Windham County Medical Association, the Connecticut Medical Society, the American Medical Association, the American Society of Abdominal Surgeons, and the American Flying Physicians Association. He was also a member of many civic organizations. Dr. LaPalme died June 7, at the age of 48.

Perham, William S., New Haven; Michigan University School of Medicine, 1932. During World War II, Dr. Perham served as captain of orthopedic surgery for the 39th General Hospital. He was associate professor of orthopedic surgery at the Yale Medical School and acted as chief orthopedic surgeon for the Yale University Health Department. He was also chief orthopedic surgeon at St. Raphael's Hospital. Dr. Perham was a member of the American Board of Orthopedic Surgeons, and a Fellow of the American Academy of Orthopedic Surgeons. He was also a member of the New Haven Medical Society, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Perham died August 1, at the age of 62.

Rose, Samuel A., Stamford, New York University School of Medicine, 1920. Dr. Rose was a prominent cardiologist in the Stamford area for over 40 years. During World War II, Dr. Rose served in the Army Medical Corps. He was a cardiology consultant at the Stamford Hospital and St. Joseph's Hospital. Dr. Rose was a former president of the Stamford Medical Society, vice president of the Connecticut Heart Association, and a founder of the Stamford Heart Association. He was a member of the Stamford Medical Society, the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, and a Fellow of the American College of Physicians. Dr. Rose died July 16, at the age of 69.

Sciortino, Michael V.—Bridgeport, University of Naples, 1937. Dr. Sciortino was a general practitioner in the Bridgeport area for over 20 years. He was associated with Park City, St. Vincent's, and Bridgeport hospitals. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Academy of General Practice. Dr. Sciortino died May 31, at the age of 57.

Troy, John W., Gales Ferry; Georgetown University School of Medicine, 1947. Dr. Troy was retired from the U.S. Navy having served in World War II and the Korean conflict, and was a general practitioner in Gales Ferry. He was a member of the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Troy died April 10, at the age of 44.

Doctor's Office

Ned Hickmon, M.D., announces the opening of an office for the practice of obstetrics and gynecology in the Woodland Medical Center, 140 Woodland Street, Hartford.

Arthur Mostel, M.D., announces his association with Robert Madison, M.D. in the practice of obstetrics and gynecology at 27 Strawberry Hill Avenue, Stamford.

Leland M. Wight, M.D., announces his association with Pediatric Associates of New Haven for the practice of pediatrics and pediatric cardiology at Doctor's Building, 2 Church Street, South, New Haven.

Robert Turfboer, M.D. announces that during his leave of absence, his office for the practice of psychiatry at 300 Amity Road, Woodbridge, will be closed from September 25, 1968 till April 1, 1969.

BOOKS RECEIVED

Familiar Medical Quotations. Edited by Maurice B. Strauss, M.D. Little, Brown and Company, Boston, 1968. 968 pp. $15.00.

Growth of the Nervous System. A Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1968. 295 pp. with 101 illustrations. $12.00.

Systematic Mycoses. A Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Ruth Porter. Little, Brown and Company, Boston, 1968. 287 pp. with 49 illustrations. $12.00.

WOMAN'S AUXILIARY

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Mrs. Edwin R. Connors, Hartford

Membership

There is perhaps no aspect of the work of the Woman's Auxiliary which is so important and about which so much has been written as membership. The writings and discussions of the problems of maintaining a membership are usually reduced to two areas, retaining present members and gaining new ones. Most people who have done any organizational work at all are aware that this is a problem of any group. And that a group is usually divided into separate lists: the inactive, the partially active, and the inner core which spearheads all important activities.

The problems of membership have not changed over the years; nor have the solutions. Different counties offer different activities to introduce new members of the county to others and to stimulate interest in the auxiliary and its work. Perhaps we need some new ideas, but there is no new idea which will surpass the individual, person-to-person touch of inviting someone to go to a meeting as your guest.

Our times are such that each person who is willing to do volunteer work is besieged by many organizations. And if a woman has children she is expected by society to be interested not only in her own activities, but in her children's, leaving her pulled in many directions in trying to satisfy her family, herself, and her community. If she is a doctor's wife, she is certainly expected to support her husband's hospital.

But what is there that only a doctor's wife can support? The auxiliary to her husband's medical society. Surely its programs are varied enough to encompass every woman. The need is there for the doctor's wife to participate in the dissemination of information about community health, mental health, safety, health careers, etc. Medicine is still and always will be surrounded by an aura of mystery and drama as far as the lay public is concerned. This aura is essential and should not be broken down, but by being set apart in the community, the doctor's wife can use her position to teach the public. While the doctor is busy with his daily practice, his wife through her auxiliary work may offer programs which will help her area. It need not be anything on a grand scale with much publicity. Who knows if merely taking the time to set up a display of posters in a library might teach someone more about health? Or if participation in a health career's hospital visit by high school students might direct some young person into the health field? Or if earning money for a nursing scholarship might add a nurse to the hospital staff in a few years?

The auxiliary also has its social aspect for its members. Fairfield county at one time had a golf chairman, and Windham county this past year held several daytime bowling parties. Novice and experienced bowlers enjoyed a morning of companionship and exercise followed by lunch in a nearby restaurant. Some county medical societies and auxiliaries hold their meetings at the same times so husbands and wives may enjoy dinner together in good company. Various fund raising events such as dances, travel programs and musicals add to the social nature of the organization. Annual meetings of the state auxiliary have also provided us with interesting speakers on such varied subjects as cooking (Poppy Cannon), underwater sea exploration (Capt. George Bond, USN), sex education (Dr. Humphrey of UConn), and Dr. William Walsh, founder of project HOPE. Fur and dress shows have also added a spark of interest.

We want every doctor's wife to join us; not only to help in the work, but to increase the fellowship and the feeling of belonging and understanding such as she can get no where else.

Several months ago *MD's Wife*, the publication of the Woman's Auxiliary to the American Medical Association, requested a card from the readers about the magazine. I thought I would make the same request, because I have wondered who reads this column in CONNECTICUT MEDICINE. Do the doctors read it, when they have so much medical reading to keep up? Do their wives read it, auxiliary members or not? Or is the magazine left at the doctor's office, and never reaches the woman who doesn't know we need her? If someone has the time and interest to drop me a card of comment, I would be very pleased.

Write to:

Mrs. James F. Jones
Green Hollow Road
Danielson, Conn. 06239

IN MEMORIAM

Mrs. Fred B. Agee—Wethersfield
Mrs. Theodore Bevans—Waterbury
Mrs. Carl Harvey—Middletown
Mrs. Lewis P. James—West Hartford
Mrs. Fritz Meyer—Bridgeport
Mrs. Arthur F. Roche—West Hartford
Mrs. William Tate—Deep River
Mrs. Alfred Vandersluis—Waterford

Placement Wanted

PHYSIATRIST—NYU trained in physical medicine and rehabilitation, Connecticut and New York licenses, seeks full-time or part-time position in Connecticut.

SURGEON—38 years of age, Board eligible, with National Boards, wishes to practice in association with another surgeon. Available immediately. Excellent training.

ORTHOPEDIC SURGEON — 37 years of age, Board eligible, military obligations completed. Wishes to practice with an associate or a group, available as of January 1, 1969.

OBS-GYN—13 years practice, Washington, D.C. Has Obs-Gyn, plus F.A.C.S. and F.A.C.O.G. Wishes to relocate in association in the New Haven area. Has Connecticut license.

PEDIATRICIAN—32 years of age, Board eligible with National Boards. Wishes to establish himself with a group or associate practice about September or October, 1968. Presently completing military obligations.

INTERNIST—Board eligible with cardiology subspecialty; 14 years private practice in Connecticut, also administrative and teaching experience. Will consider group, hospital or industrial position; clinical or administrative.

INTERNIST — 41 year old internist-cardiologist seeks association with group, industry or institution. Has special training, also, in chest diseases and dermatology. Connecticut license.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

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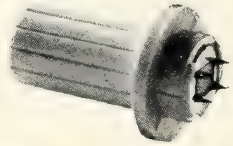

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MEETINGS

BASIC SCIENCE

Recent Advances in Clinical Physiology

Tuesdays, 7:15 P.M., September 10—June 10, 1968

Lawrence and Memorial Hospitals Auditorium, New London

Seventh series of courses (20) in basic science as related to clinical medicine; participants granted 40 hours of post-graduate credit by the Connecticut Academy of General Practice. Registration limited to 75; fee $100 for the 20 seminars. Director, Edward Gipstein, M.D., Director of Medical Education, Lawrence and Memorial Hospitals and Chief, Department of Medicine. Co-Director, Richard Gorlin, M.D., Senior in Medicine and Director of Cardiovascular Research, Peter Bent Brigham Hospital, Boston. Speakers from Peter Bent Brigham Hospital and Harvard Medical School.

MEDICINE

September 25 8:30 A.M. to 5:00 P.M.

17th Annual Scientific Symposium, Connecticut Academy of General Practice

Park Plaza Hotel, New Haven

Panel Presentation, "The Coronary": Joseph E. F. Riseman, M.D., Assistant Clinical Professor of Medicine, Harvard Medical School; J. Scott Butterworth, M.D., Associate Professor of Medicine, New York University School of Medicine; Louis A. Soloff, M.D., Professor of Medicine, Temple University, Chief Division of Cardiology.

Panel Discussion, "The Right to Live and Die": John Donnelly, M.D., Psychiatrist-in-Chief, Institute of Living, Hartford; Cyril F. Jones., M.D., Clinical Assistant Professor of Surgery, Downstate Medical Center, State University of New York; George A. Friedman, M.D., L.LB, Medical Legal Consultant, New York; Don Browing, Ph.D., Professor of Religion, University of Chicago Divinity School; Cyril H. Wecht, M.D., L.LB., Clinical Instructor in Pathology, University of Pittsburgh School of Medicine.

Luncheon Speaker, Lewis Miller, Editor, Patient Care Magazine.

Topic: "Will There Be a Family Physician in the Future?"

Contact Rudolph A. Damiani, M.D., c/o Academy Executive Office, 179 Allyn Street, Hartford, or 246-6566. No registration fee; open to all physicians.

PSYCHIATRY

Fall series beginning mid-September

Psychiatry for Non-Psychiatric Physicians

Case centered seminars with up to 10 practitioners per group. Eight to 10 weekly sessions at locations around the state.

Sponsored by the Connecticut Academy of General Practice and the Connecticut Branch of the American Psychiatric Association.

Contact: Stephen Fleck, M.D., Department of Psychiatry, Yale University School of Medicine, 333 Cedar Street, New Haven, or 562-1161, Ext. 617. No registration fee; open to all physicians.

Seminars sponsored by the Connecticut Valley Hospital at Merritt Hall Auditorium

September 10 2 P.M.

"Psychiatry In Our Time", Francis J. Braceland, M.D.

September 17 10:30 A.M.

"Psychodynamics in Clinical Psychiatry," Oscar K. Diamond, M.D.

September 25 10:30 A.M.

"Psychotherapy of the Psychoses," Nolan C. D. Lewis, M.D.

October 22 2:00 P.M.

"The Progressive Changes of Psychoanalysis in Modern Psychiatry," May E. Romm, M.D.

SURGERY

September 20 3:00 P.M.

Seminar on Therapeutic Contact Lenses

Fitkin Amphitheatre, Yale-New Haven Medical Center

Sponsored by Section on Opthalmology of both the Connecticut State Medical Society and the Yale University of Medicine

Participants: Leonard Flom, M.D., and staff of Contact Lens Clinic, Yale New Haven Medical Center; Philip Salvatori, President of Obrig Laboratories, who will speak on and demonstrate techniques of flush fitting and minimal clearance seleral lenses.

Contact: Leonard Flom, M.D., Fairfield

Open to all ophthalmologists, including members of the Eye Section, CSMS

October 9 1:30 P.M.

Congenital Opthalmological Anomalies

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Third Annual Combined Clinical Meeting of Section on Ophthalmology, Connecticut State Medical Society and Yale University Medical School.

1:30 P.M., Yale New Haven Medical Center Eye Clinic for patient examination; 3:30 P.M. discussion and business meeting, Brady Auditorium; 6:00 P.M. social hour and dinner, Park Plaza Hotel.

Participants: Harold F. Falls, M.D., Professor of Ophthalmology, University of Michigan School of Medicine; Rufus Howard, M.D., Assistant Professor of Opthalmology, Yale University School of Medicine.

Contact: Dewey Katz, M.D., Hartford; Rufus Howard, M.D., Yale New Haven Hospital.

Open to all ophthalmologists, including members of the Eye Section, CSMS.

GENERAL

October 24 3:30 P.M.

185th Semi-Annual Meeting of the New Haven County Medical Association, Waverly Inn, Cheshire

October 5-6

Second National Congress on Medical Ethics, sponsored by the Judicial Council of the AMA
Drake Hotel, Chicago

September 1-6

American Society of Hematology
Waldorf-Astoria, New York

September 5-7

American Association of Obstetricians and Gynecologists
The Homestead, Hot Springs, Va.

September 13-20

American Academy of General Practice
Las Vegas, Nevada

September 16-19

American Hospital Association
Atlantic City, New Jersey

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AMA Offers Flier On Smoking-Health

As an additional cautionary reminder about the health effects of cigarette smoking, the AMA has published a new Timely Tip — "The Cigarette — A Dubious Companion."

"The Cigarette — A Dubious Companion" describes the effects of each puff of smoke as it enters the breathing passages and air sacs of the lungs and stresses that certain conditions and diseases are believed to be aggravated by cigarette smoking.

Some physicians include AMA Timely Tips in their mailings and offer them in their reception rooms.

There are 100 Timely Tips to a set. Copies are available from the AMA Order Department at 20 cents each for 1-4 sets and 15 cents each for 5 or more sets.

The Connecticut State Medical Society offers placement assistance through the Physician Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

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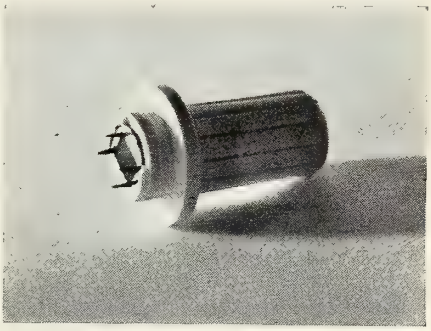

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Connecticut Medicine

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The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the Journal (listing name and initials of author, title of article, journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

ILLUSTRATIONS

Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration as well as typed on a separate sheet. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. Connnecticut Medicine will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

NEWS

Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

ADVERTISING

All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by Connecticut Medicine.

Material other than original articles should be received not later than the 10th of the month PRECEDING date of issue.

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Reprint orders should be returned at once as the type will be destroyed immediately following publication of the manuscript. The Journal does not stock reprints of the articles published. Requests for individual reprints should be sent to the author.

Communications should be addressed to Connecticut Medicine, 160 St. Ronan Street, New Haven, Conn., 06511 Telephone 865-0587.

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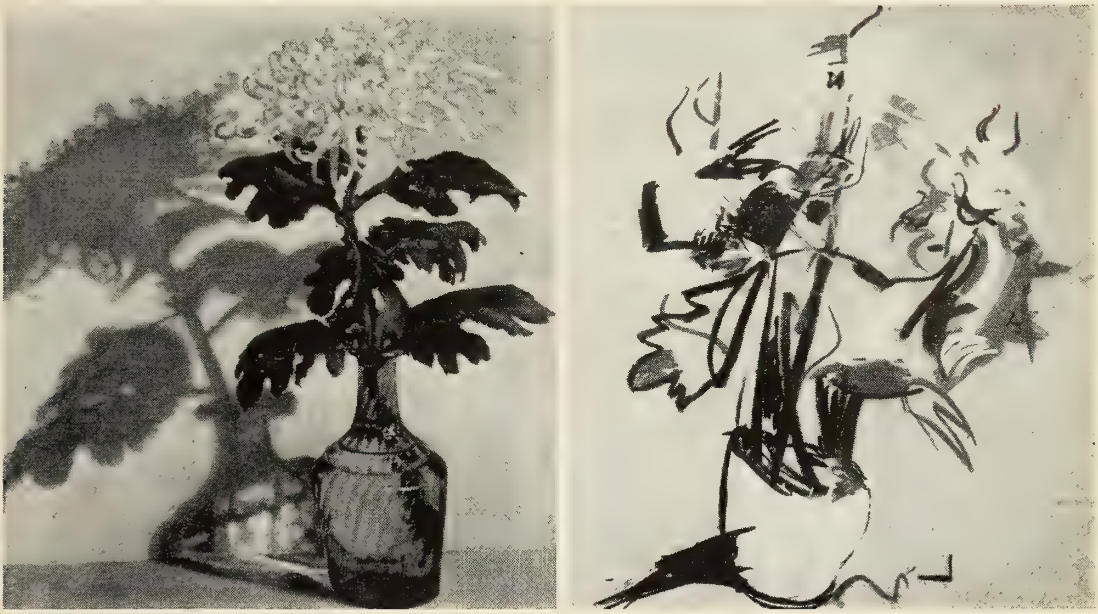
Connecticut Medicine

Connecticut State Medical Journal

Volume 32 / October 1968 / Number 10



Normal painting

Same subject by the same artist under the influence of LSD

Artist, Jack Jones, Santa Monica, California

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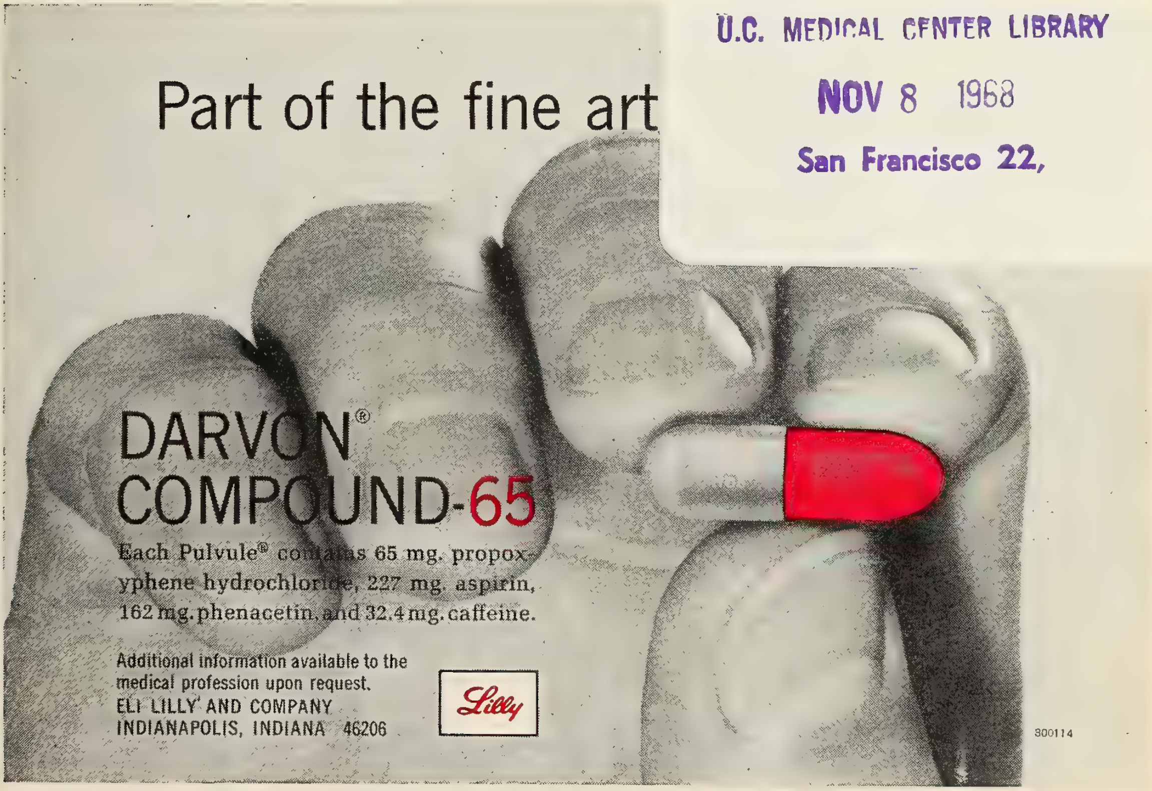

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Connecticut Medicine
OCTOBER, 1968
Vol. 32/No. 10

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County of New Haven ss.

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LOUIS H. NAHUM, M.D.
Editor,
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ABOUT THE COVER

Dear Dr. Nahum:

. . . "At the time I was given LSD by Dr. Cohen for the purpose of this experiment in creativity very few negative experiments had come out of the research, which was usually conducted (1) by experienced investigators (2) in carefully controlled environments and (3) with positive expectation on the part of the experient. In the group in which I took LSD four times over a space of about eight years (that group which usually included the philosopher Gerald Heard) there were no disasters and almost no negative experiences. Everyone, even the one or two who partially explored the 'hell' regions by choice, felt deeply moved, more than by any other experience in adult life. This is why I feel the truth should now be told about the pictures.

There were four, only *one* of which was an attempt to translate the oil painting of the chrysanthemum into terms of pastel technique (in about 20 minutes!) and ironically this one has never been published. It was cut off from the color photo of the four pictures which was printed in the TIME book. The best composition, the most pleasing aesthetically was the one reprinted in *Science.* This was the first picture done, early in the experience while the attention was still willing to 'stick to the job', for as you know the vast world of psychophysical consciousness is blooming before one's awareness so that the last thing one wishes to do is to scrawl with pastels. The *Science* cover picture really is the most interesting of the four and a valid comparison can be made between it and the oil, for I chose a white plastic flowerpot in which were growing at least six yellow spider chrysanthemums, exactly the same kind and size which I used for the oil painting of the single 'mum in the Mexican blue glass vase. At no time did I believe I was making an exact copy, for I was quite conscious of my waning attention to the job at hand. I was much more interested in talking to my invigilator. I took copious notes immediately after the experience (that night) so I do not have to depend on my memory for this. He and I were laughing till I had to hold my sides because I had always had an abhorrence of abstract expressionist art (I no longer do) and yet every line I put down on the paper looked terribly like just that.

The captions in both the TIME book and the *Science* hold that I used the oil painting "as a model" for the pastel pictures they printed and that I believed "the copies were exact" and that I "was painting an excellent piece." This is very far from the truth, as I think you will see is obvious from a short study of the picture. The black triangle on the lower left of the *Science* cover is the shadow cast by the white plastic flowerpot, which was standing on a green asbestos tile floor, one tile of which is suggested by the "backward L" on the lower right. The other dark lines are either stems of the chrysanthemums or lines defining shadows or the fanning edges of leaves. The "stringy" light lines and areas (yellow in the original) in the upper two-thirds of the picture suggest the long spidery petals of the chrysanthemums. The *movement* of the masses, emphasized by the tilting flowerpot, is quite uncharacteristic of my usual work, even now. I would feel (now and also then) that this easy solution to pattern (dismissing the arduous study of natural appearances as unnecessary) is somewhat "dishonest," though at the time it was great fun, as I said.

Curiously, the real pastel *copy* of the oil is "closer" to me personally because by that time the joyous lack of concern with the *persona* (the surface "mask" of the ego) had completely taken over and even the artistic improvisation become more surreal (the shadow, for instance, instead of a regular flower shadow sprouts its own yellow blossom). Still, I do believe, as does Dr. Cohen, that the *Science* cover is the best example and comparison with the oil." . . .

My respect and best wishes,

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Connecticut Medicine

editorials

The New Objectives In Medical Education

The United States has experienced three revolutions in medical education. The first one occurred in the 18th and early 19th century when training doctors by apprenticeship gave way to the development of medical schools with a formal curriculum. In the early 20th century the Flaxner report ushered in the second revolution. Full time faculty devoted to research as well as teaching gradually replaced the practitioner as teacher. At the same time, the standard four year curriculum was instituted throughout the country. We are now in the third revolution which is reaching major proportions. The curriculum is now undergoing revision in nearly every medical school. What has brought this about and what are the changes that are taking place and will continue to take place?

As we view the ferment in medicine we can discern at least three major factors that have accelerated the changes in medical education. One of the most important is the great progress in the field of cell biology and biomedical science in general. Medicine accordingly is now able to use much of the new information in biology so that medical practice is rapidly changing from an art to an applied science. The growth in specialized skills has accelerated the trend towards specialization. This compels adaptation of the curriculum. Presently over 80 per cent of all graduates in medical schools are going into residencies in the various specialties of medicine and surgery. A majority of the remainder are taking additional training in family medicine. Thus the period of post-graduate education is the equal to the time spent in medical school for the majority of our graduates.

Another important factor demanding changes in medical curriculum away from the rigid four year course, divided formerly into two preclinical and two clinical years is the increased sophistication of the student entering medical school. He is better prepared in the biological and physical sciences at the high school and college level[1]. The new student is insisting on greater individuality and better ways for integrating premedical and medical education. Some students are much better prepared in some areas such as biochemistry, physiology, genetics and cell biology but not at all in gross anatomy and neuroanatomy. Even in prepared areas there is wide variability among the students[2]. Accordingly attempts are being made to determine individual educational differences and special areas of interest. This requires individualization of curricula appropriate for each student.

A third major force for changes in medical education comes from society and the student body itself. The pressure for better medical care for all must influence the way doctors are to be educated. Experimentation with newer ways of making medicine available to all has received great impetus from Medicare, regional medical programs, active demands from the organized poor, as well as other social forces. This has become the responsibility of the medical schools. What is more, the student is becoming more articulate in his insistence upon the opportunity to participate in these programs. The student body is also insisting on greater individuality in the form of a more flexible curriculum. It is therefore particularly important for the faculty and for practicing physicians to understand the need to revise the objectives of medical education.

How are these changes being brought about? One is the search for better ways to integrate premedical with medical education. Attempts are being made to determine individual educational differences and special areas of interest and develop a curriculum that will be most appropriate for each student. In part to accomplish this, the traditional courses in basic sciences have been reduced to their "core" content. A third change is a shift to a more flexible curriculum by offering electives and "tracts" or majors. A fourth major shift has been the introduction of new subjects. In basic science, emphasis is on cell biology. In clinical years programs on community medicine, comprehensive health care and family practice.

In Colorado[3] for example, identifying the "core" content from the great mass of biological scientific information has been solved by simply reducing the course time by 30 per cent for all departments that teach in the first two years. It is then up to each individual department to attempt to define the core material. The electives and majors have been solved in this school by not scheduling any major courses for freshman and sophomores on Monday, Wednesday and Friday afternoons to make time available for electives or independent study. They anticipate that many students will take clinically oriented electives in the first two years thus allowing early patient contact. When seniors do this, they will probably select courses in the basic sciences. The senior year will be all elective thus providing an opportunity to specialize or to prepare for family medicine or public health or community medicine. In these ways the student can pursue his areas in greater depth.

These changes in the objectives of medical education occurring throughout the country will require new methods of evaluation of student progress to allow appropriate credit for the individualized curriculum. The student is now being prepared academically to proceed with graduate training. He is being educated as a scientist rather than a technician. Self-learning is being emphasized in order to prepare the individual to continue his own education. The rigid mold has fallen away and given way to individualization. Throughout it all will prevail a true academic atmosphere.

We will now require a special development of certification and licensure examinations. If the student is to be given the opportunity to pursue certain basic sciences and clinical areas in depth than others, it is important that he be not handicapped by the necessity to pass examinations in individual subjects with the same minimum score. This means that the National Board of Medical Examiners and the State Licensing agencies will have to reorient their appraisals in this direction[4].

L.H.N.

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LSD and Marihuana

It is probable that the use of psychedelic drugs would not have become so widespread had not the press glamorized them. Fank Barron has said: "The chemical substance most instrumental in the spread of the psychedelic movement is printer's ink. . . . Although the press deplores the excesses they are at pains to picture and warn of dangers, then at the same time suggest the appeal of what they dramatize." Today psychedelic drugs are being tried by a substantial fraction of the best of our nation's youth. The current favorite among university students is marihuana. At a recent symposium held at the College of Physicians of Philadelphia, Dana F. Farnsworth of Harvard reported that 30 to 35 per cent of the students of major universities in the East and West coasts had tried marihuana at least once. About half of the students did not repeat the experiment. Even so 15 to 20 per cent did[1].

Farnsworth also reported that 5 per cent of the students had tried LSD at the height of its popularity several years ago. Current use is probably under 1 per cent. He attributed this decline to an awareness among students that the drug has untoward effects, such as schizophrenic reactions, paranoid reactions, psychotic depression, chronic anxiety reaction, and even acting out of suicidal tendencies. Louria[2] described observation on LSD induced psychosis and LSD causing exacerbation of an established psychotic disorder. About a sixth of his patients had not recovered after two weeks and were referred for potential long-term hospitalization. Chronic abuse of LSD often leads to a "solipsistic negativistic existence in which LSD becomes synonymous with life itself." Although students are aware of at least some of these mental effects they are more impressed by reports of chromosomal damage and possible birth defects arising from the use of this hallucinogen. Such reports have had a sobering effect exceeding that of any preaching by adults.

While the use of LSD seems to be decreasing, the use of marihuana appears to be growing, both in high schools and in universities[3]. The inconclusive information about marihuana is not reassuring. This is so because the social setting in which "pot" is used is conducive to other more serious adventures such as going on to other drugs like LSD, heroin, amphetamine and barbiturates. Some of the effects of marihuana seem reminiscent of LSD. Large doses produce confusion, disorientation and increased anxiety and psychoses lasting hours and sometimes weeks. In the Middle East habitual use of marihuana leads to a cannabis psychosis whose victims are reminiscent of the derelicts of skid row.

Now that the drug has become popular with an appreciable number of young people in the middle and upper socio-economic classes, there has become a need for a clear statement by competent and recognized authorities as to whether it is harmless as some "experts" far distant from pharmacology and medicine claimed. After appraising all avail-

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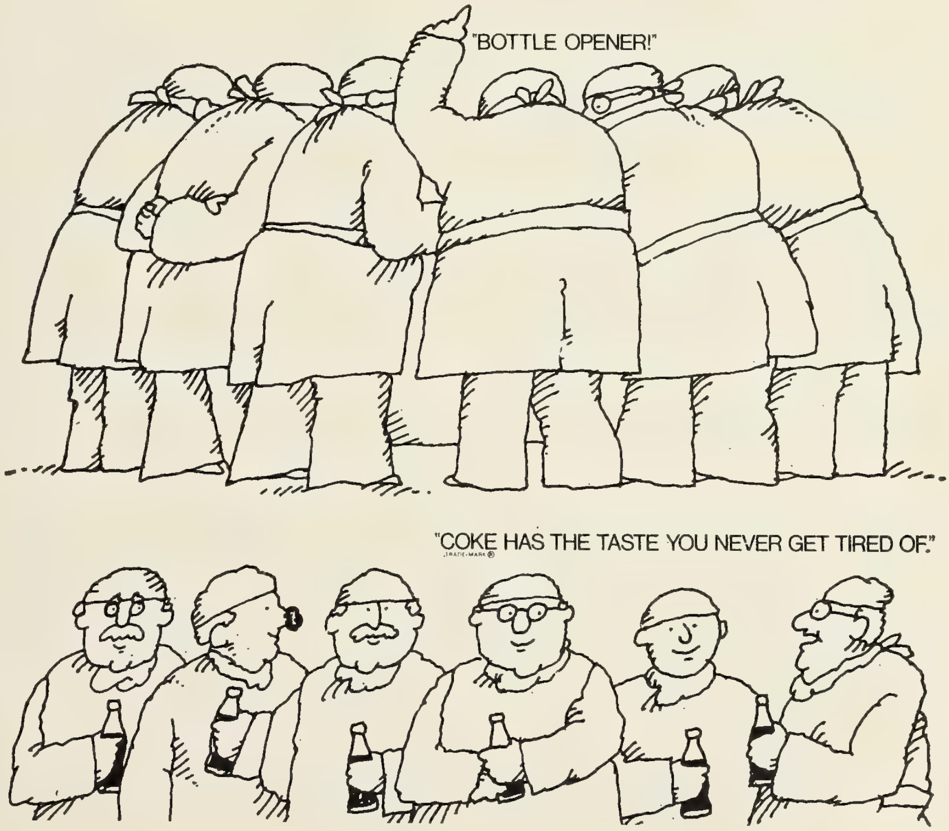

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able information concerning cannabis the Council on Mental Health of the A.M.A.[4] has concluded that it is indeed a harmful drug and that its legalization would lead to even more serious medical and social consequences that now result from its use.

The harmfulness of marihuana both to the individual user and to society too often is masked by the manner in which the drug is used in this country. Casual episodic use is the pattern and furthermore the strength of the drug typically is not of the magnitude found elsewhere in the world. For these reasons most Americans do not suffer lasting physical and psychological impairment and do not exhibit strong dependence on the substance. Some, however, do become chronic users with concomitant medical and interpersonal problems. The greater proportion of users are introduced to marihuana out of curiosity, youthful thrill-seeking, a desire to be "in" and a wish to demonstrate independence from a generation who is addicted to another drug, alcohol.

The relatively minor effects of weak marihuana preparations often give the false impression that any drug can be "handled". However, marihuana interferes with ones doing what he wants to do and should do and at the same time prevents his caring that he is not doing it. It produces a wish fulfilling fantasy of omnipotence and gives the illusion of intimacy without responsibility. Conversion of knowledge and attitudes into patterns of acceptable behavior is prevented. Thus at the very time when the young people are being called on to make important career and other lifemolding decisions we are seeing a substantial number of them becoming drug oriented in addition to those who are already drug dependent, inevitably blocking constructive action and leaving damaging long term effects. The real harm to society derived from the abuse of cannabis rests upon the consequences of the impairment of the individual's social function and his enhanced proneness to asocial and antisocial behavior.

Even though cannabis is a dangerous drug and as such a public health concern, legalization would create a serious abuse problem. Already the penalties for violations of the marihuana laws are too harsh and too unrealistic. For example: possession subjects a person to penalties of 2 to 10 years imprisonment on the first offense, 5 to 20 years for the second and 10 to 40 years for additional offences. While persons should not be allowed to become involved with marihuana with impunity, legislators, law enforcement officers and the courts should differentiate in the handling of an occasional user from the chronic user, the person sharing it with another and the dealer who sells it for a profit. If the purpose of imposing penalties is to deter acts which might injure the individual and disrupt society, then equitable penalties insofar as they enhance respect for the law can contribute to effective prevention and facilitate rehabilitation of the offenders.

An informed citizenry in the final analysis is the most effective deterrant of all. Accordingly educational programs with respect to dangers of drug abuse should be directed to all segments of the population. Primary and secondary schools as well as colleges and universities should establish such programs. It would be well if communications media disseminated authoritative information. Physicians especially should call attention frequently and forcefully to the problems created by drug abuse and drug dependence[5, 6].

L.H.N.

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Air Pollution And Emphysema

About 20,000 Americans will die of emphysema this year, seven times the number that succumbed to it a decade ago. It disables one out of fourteen American workers over forty-five years of age. E. Cyler Hammond,[1] Vice President of the American Cancer Society told a senate subcommittee that a recent study of 126,000 men indicates that a combined atmosphere of cigarette smoke and occupational pollution creates heigthened risk of emphysema. A nonsmoker exposed to occupational pollution (smog, pollen, dust, exhaust fumes or other irritants) has one chance in ninety of developing emphysema. Among heavy smokers exposed to the same air pollution, one in seven develops this crippling disease. These findings are not new and are supported by those of others that air pollution and cigarette smoking often leads to destruction of lung tissue that characterizes emphysema.

The site and nature of the airways of obstruction in human lungs has recently been clarified by Hogg, Macklem and Thurbeck[2] by measuring pressure in the small airways (bronchi less than 2 mm. in diameter) in excised human lungs. A major advantage of their method is that morphologic studies can be carried out immediately and correlated with physiologic findings. A major disadvantage, of course, is the uncertainty whether the excised lungs behave in a way similar to that of the intact human lungs. In normal lungs only about one-quarter of the total resistance is in airways smaller than 2 mm. in diameter. In diseased patients, however, it is the peripheral airways which are the major site of resistance in obstructive lung disease. This appears to be true not only in emphysema, but also in bronchitis and bronchiectasis.

In the normal lung, airways are tethered and supported by alveolar walls which extend radially like the spokes of a wheel from the outer wall of the airway. In emphysema with destruction of the alveolar walls, the bronchioles would lose their support. In this situation the outer walls of the bronchioles would be subjected to alveolar pressure and would easily collapse during expiration when their intraluminal pressure was less than alveolar pressure. Butler et al[3] have in fact shown that airway resistance increases as elastic recoil decreases. Since emphysema is characterized by a loss of elastic recoil, the airway obstruction could be secondary at least in part to this obstruction. Hogg has found that there are in fact two sites of airway obstruction, one in the large airways which is due to dynamic compression of these structures and therefore present only in expiration. The other in the smaller airways which is present during both inspiration and expiration.

Hogg's studies further reveals that in patients with obstructive disease of the airways a large increase in the resistance in the small airways must occur to be detected by conventional tests of pulmonary function such as maximum breathing capacity or the forced expiratory volume. As a corollary he raises the possibility that early in the natural history of emphysema a fair amount of obstruction exists in the small airways, while insufficient to be detected clinically or by physiologic testing, is nevertheless enough to derange the distribution of ventilation and alveolar capillary gas exchange and of course produce the sensation of breathlessness.

The changes found in diseased small airways have two distinct components, one potentially reversible and the other irreversible. The reversible component is related to mucus plugging and acute inflammation of the airways. This is the morphologic counterpart of the characteristic exacerbations from which patients with chronic bronchitis suffer and is certainly treatable. The irreversible component is related to fibrosis, distortion and narrowing and obliteration of small airways representing fixed obstruction. The relative contribution of these two components needs further quantitative studies. There is, however, a strong likelihood that at some stage emphysema causes significant abnormalities in the distribution of ventilation and presumably in gas exchange but is undetectable by either the direct measurement of airway resistance or its indirect assessment obtained from examination of forced expiratory volume and flow rates.

The clinician, of course, now has to deal with eliminating infectious and mucus plugging which have shown to be reversible. He must also recognize the importance of the factors in our environment which so importantly contributes to the development of emphysema and chronic lung disease such as inhaling polluted air from the environment, and from cigarette smoke. Sometimes it means that the patient must change jobs or places of residence. It always means giving up smoking and avoiding smoke filled rooms.

L.H.N.

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The Possibility Of Living Again After "Death From Lightning"

Taussig[1] after seeing a young boy struck by lightning, thrown to the ground and burned, but recovered confesses "how little I knew about the possibility of resuscitating a person "killed" by lightning." Of the numerous reports from all over the world about people "killed" by lightning, she was able to find only one, that by Ravitch et al[2] in which a successful effort was made to revive the dead. This report dealt with a ten year old boy struck by lightning while riding a bicycle. The boy was found unconscious slumped on his bicycle against a tree. He was carried to a school where a boy scout felt a pulse and proceeded to carry out artificial respiration. Twenty-two minutes later he was apparently dead at a hospital. He didn't breathe and had not received artificial respiration for seven minutes. His pupils were dilated, lips cyanotic and he was pulseless. Mouth to airway respiration was instituted and the chest opened. The heart was motionless, cardiac massage was begun, epinephrin injected into the left ventricle. In five minutes heart action was started, hypothermia instituted. He was placed in a respirator where he remained for three days. He was comatose for six days. He was discharged from the hospital twenty-nine days later completely recovered except for nasal speech and a slightly higher I.Q.

Several questions are raised by this experience. Knowing that the brain dies after four minutes of oxygen lack why was it this boy survived without respiration or heart beat for over twelve minutes and probably longer? When the heart was started why did it not go into ventricular fibrillation but remained in regular sinus rhythm? We know that ventricular fibrillation is common in a person electrocuted by a high tension wire. Why have people accepted "death" from lightning merely because respiration ceased and the heart stopped without any serious efforts being made at prolonged resuscitation.

The current from lightning is much more powerful than that from a power wire[3] and in fact closely resembles that from a defibrillor because when the heart starts it also does so with regular sinus rhythm as if it had been defibrillated. Apparently when a person is struck by lightning, the heart action, respiration and all metabolism ceases instantly. This cessation of metabolism includes the brain cells so that apparently the onset of degenerative processes is delayed, we know not how long. But the time interval between death and resuscitation is far longer than in almost any other known circumstance. Knowledge of this fact should in the future encourage prolonged efforts at resuscitation of all people "killed" by lightning.

There are of course many more people struck by lightning that survive than those who are killed. In West Germany from 1952-60, 331 persons were reported killed and 409 non-fatal cases. Marriott in 1951 reported a church in East Africa with a congregation of 300 was struck by lightning, only six were killed while 100 were rendered unconscious. The only figures in this country are those of the Metropolitan Life Insurance Company in which 300 persons are said to be killed by lightning per year.

Of those not killed some are rendered unconscious but can get up again soon. A rare case of myocardial infarction and several who developed electrocardiographic changes have been reported.[4] Many have burns of various intensities in association with unconsciousness and various fractures including the skull. Eye injuries are relatively common either from light energy or from electrical energy producing corneal lesions, cataract iridocyclitis hemorrhages in the vitreous.

A typical story throughout the literature is that of a person, couple or group who have taken shelter beneath a tree or under a shed. The person is knocked unconscious and thrown to the ground. He may be thrown with such force that he suffers injury such as fracture of the skull or broken bones. When he regains consciousness his extremities feel dead and he is unable to move.[5] His extremities are either white or cyanotic and pulseless. Gradually sensation, numbness and tingling returns and eventually he regains use of his limbs. Not infrequently the person is mute and unable to speak when he first recovers consciousness. The person may show burns of various types and degrees of severity. However, they seldom require skin grafting. All evidence indicates that loss of consciousness is instantaneous and then followed by retrograde anmesia. Some will remember a flash without hearing the thunder and other remember neither. Pliny is credited with the saying that "he who sees the lighning and hears the thunder is not the man who has been struck."

The two most serious complications are the eye or ear. Deafness may be caused by the blast of an unheard clap of thunder and various types of injury to the eye may occur. However, except for these possible complications of deafness and blindness or other impairment of vision recovery if it occurs is usually complete.

There are now clear rules about prevention. Respect a severe thunderstorm. Don't take refuge under a tree. Cast aside your fishing rod, your golf clubs and even your umbrella. Don't run, don't telephone, don't go swimming. Just lie flat on the ground but away from trees or poles. If you have a raincoat lie on it. If indoors don't stand between an open door and an open window, as lighting may strike horizontally between the door and window along a current of hot or moist air. Most important of all is for us to realize that a person who has been struck by lightning who is stunned but alive is not the one who most urgently needs help. Such a person will probably soon recover.

It is the man who is "dead" with no heart action and no respiratory movements who needs cardiopulmonary resuscitation. When the heart starts, continue artificial respiration until the man is brought to the nearest hospital. Taussig has eloquently stated "he has traveled on one of the two way streets to heaven. Although his trip to heaven was instantaneous and his trip back may take days or weeks he may yet return to life and what is more the chances are that he will be uninjured by the trip." The lesson we learn from "death" by lightning is that a person "killed" by lightning is not necessarily dead even though he is without respiration, without pulse and without consciousness for relatively prolonged periods. This lesson is especially important now, when new definitions of death are being formulated in many centers.

L.H.N.

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New Concepts On Viral Hepatitis

During the past decade advances in virology and vaccine development have resulted in a striking decline in the incidence of a number of common viral diseases especially measles and poliomyelitis. However, progress in hepatitis virology has been exceedingly slow. At present the etiologic agent of viral hepatitis has not been identified and no vaccine is available for the prevention of the disease. Viral hepatitis, however, has attracted increasing attention as a public health problem because of its widespread prevalence and high incidence. For example in the week of July 6, 1968, there were

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reported to the U.S. Department of Health, Education and Welfare, 759 cases of hepatitis as compared to 593 in the same week of last year.

At present a major public health goal is to work toward the prevention of viral hepatitis based on a sound knowledge of the epidemiology of the disease. Over the past few years a number of studies have led to important conceptual changes in the epidemiology of viral hepatitis. Attempts at isolation of the etiologic agent have resulted in the isolation of a number of agents from patients with hepatitis but thus far their etiologic significance remains speculative. Until recently it was not possible to transmit the disease to animals. Recent epidemiologic and experimental studies suggest that non-human primates can in fact transmit the disease to man. The primate may in turn be susceptible to human hepatitis virus. For example Deinhardt and his co-workers[1] have reported that the marmoset, a small but ferocious South American monkey is susceptible to hepatitis. They transferred the hepatitis from animal to animal by inoculation of serum from the marmoset during the acute stage of the disease. We may expect from work of this kind soon to have isolation of the causative agent of viral hepatitis.

Another concept that has recently been modified is the one that serum hepatitis is a disease transmitted only by the parenteral route. There is now experimental evidence of a fecal-oral spread of this form of hepatitis[2]. However, such non-parenteral transmission of serum hepatitis is relatively uncommon since most cases of serum hepatitis can be traced to tissue penetration or blood transfusions or use of contaminated equipment.[3] Examples are sharing of unsterilized equipment for heroin and amphetamine use among adults. We may expect hepatitis will be an increasing frequent complication of such practices. Drug users often sell their blood to commercial blood banks to obtain money for drugs.

Ringertz and Zetterberg[4] described an extensive epidemic of long-incubation hepatitis among cross country track finders in Sweden caused by inoculation of virus into scratches and cuts during bathing that followed these meets. The epidemic was abruptly halted when the runners were obliged to wear protective clothing during the competition so that cuts and scratches were avoided.

There is general agreement that the risk of hepatitis increases almost linearly with the amount of blood transfused and is closely related to standards of blood selection.[5] Up to date no effective method of sterilization applicable to whole blood has been found. The calculated attack rate was 87 per 1000 units of blood transfused. It is interesting that most cases are anicteric. The ratio of anicteric to icteric cases varies with the different reports. Some believe it is as high as 100:1. In other places it is 10:1[3] and in still others it is reported as 4:1.[6] It is interesting that a large proportion of cases of post-transfusion hepatitis are due not to the virus of serum hepatitis but actually to the virus of infectious hepatitis. There are a number of reports indicating a significant risk of hepatitis for medical workers in hospital hemodialysis units. This clearly emphasizes the occupational hazard of viral hepatitis for medical and paramedical personnel.

We have learned much about the manner in which epidemics of infectious hepatitis are spread. Mostly they result by exposure to infected persons. However, ingestion of contaminated food has been implicated in some outbreaks and sporadic cases. Fecal-oral spread primarily from person to person continues to be the most common mode of transmission of infectious hepatitis in localized epidemics[7]. A history of recent contact with a known patient with hepatitis or jaundiced person is found in 30-40 per cent of patients when other sources can be reasonably well excluded. This low percentage is indicative of the significant role of the subclinical case in transmission of hepatitis. The majority of young children have either mild anicteric or totally subclinical disease whereas with increasing age the ratio of anicteric and icteric cases of infectious hepatitis approaches unity[8].

Extensive outbreaks of hepatitis traced to water or milk have been quite infrequent in this country. However, a large variety of foods contaminated during collection or preparation for marketing or consumption have been implicated in a number of epidemics. Such diverse foods as orange juice, custard, roast-pork and salad dressing have been implicated in epidemic situations[9]. Several epidemics have been traced to clams and oysters harvested from contaminated waters and then ingested raw. These may be sources of hepatitis in some communities during non-epidemic periods. Water pollution control has been seriously handicapped by lack of methods to detect hepatitis virus contamination. Furthermore even the present techniques of shellfish cleansing (defuration) may not effectively remove the virus. It is reported, however, that cationic polymers can absorb virus from aqueous suspensions and may be useful in treating virus con-

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taminated waters. This is an important area for further research.

The effectiveness of gamma gloublin in modifying infectious hepatitis is well established. Stokes long ago reported[10] a greater than 90 per cent effectiveness of a small dose 0.01 ml. per pound body weight and persists for one month for each such dose administered. The available data, however, on the efficacy of gamma gloubulin prophylaxis for post-transfusion hepatitis are conflicting.

The presence of leucocyte chromosomal abnormalities in patients recovering from infectious hepatitis and a possible association of viral hepatitis with Down's syndrome (mongolism) have been reported from Australia[11]. Such observations suggest that infection with hepatitis virus may affect cellular DNA. These findings are provocative but additional epidemiologic and cytogenetic studies of the interaction of viral hepatitis and the genetic material are needed to support these studies.

L.H.N.

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Research Related To Dentistry:

II. Bioengineering Research

Bioengineering research is that which exists between dental research and the work of a wide range of engineers, physicists and chemists. While the greatest emphasis remains in the area of materials science, there are also varied and important applications of telemetry to studies of oral health and dysfunction. The mouth functions in mastication and speech. Both involve motion of the oral structures in very intricate and purposeful patterns. Dysfunctions of the neuromuscular system of the mouth not only impair chewing and speaking but also contribute to the deterioration of oral and general health. Occasionally it will lead to trauma and pain in the temporomandibular joint. Today telemetry is providing better understanding of oral neuromuscular function in health and disease. Intra-oral and extra-oral electromyographic techniques are being used to demonstrate the contributions of individual muscles and muscle groups to jaw movements. Much materials and techniques must still be devised for this purpose.

Once tooth enamel is destroyed through dental caries or trauma a substitute material must be found for replacement, since tooth enamel cannot repair itself. The requirement of such a material are quite demanding and have been stated by Morris and Greulich to be as follows: The material must be capable of withstanding wide and rapid temperature changes and heavy loading pressures: It must be resistant to corrosive action of food and bacteria and their degradation products: It must be non soluble in saliva and, of course, esthetically acceptable. Finally its use in dental work should not require unreasonable time and skill and its cost must not be prohibitive. Significant progress has been made toward meeting these requirements, nevertheless dental treatment continues to be less than ideal because of the limitations of available material.

Morris and Greulich believe that the primary need today is for an esthetically acceptable adhesive restorative material which is plastic but hardens quickly at mouth temperatures and bonds tightly to enamel and dentin in the presence of moisture. Such a substance would require minimum preparation of tooth and its availability would substantially reduce the cost of dental care. Hope that some such ideal material will be developed is derived from the fact that just such material cements are produced by some marine plants and marine animals such as the barnacle.

The natural cements form as a liquid, harden under water, endure wide temperature changes and heavy stresses. They last for years and attract minerals from sea water so that the attachment increases with time. If such cements can be analyzed and the mechanism by which they harden under water can be explained, it should be possible to make similar substances suitable for permanent restoration of teeth.

Morris and Greulich point to the hope that some assistance in seeking the ideal material might come from the field of space technology. Here great emphasis is placed on materials science in preparation for orbital flights, long range space travel and lunar landings. For this reason workers in the dental physical sciences are closely monitoring the progress of the space program.

The loss of even a single tooth disrupts the continuity of form and function of the total masticating apparatus and leads to a sequence of inflammation and degenerative changes which threaten the remaining teeth. At present the replacement of missing teeth through fixed restorations is expensive and time consuming. The immediate insertion of a plastic replica directly into the socket following extraction of a tooth would be a relatively simple and economical procedure. Research on implantation is now receiving greater attention following promising results in experiments in which plastic teeth implanted in baboons have served for as long as six years.

Until research leads to more effective control of dental disease a large segment of the population will continue to require intraoral prothetic appliances. Currently over 20 million Americans including half of all citizens over the age of 55 have lost all their natural teeth. The acrylic resins upon which they depend for their comfort, health and social well-being leave much to be desired. Extensive resorption of bony tissue underlying dentures is common in patients who have been edentulous for several years. Investigators are trying to develop improved materials and surgical techniques for placing implants in the jaw thereby providing stable abutments upon which dentures may be seated. More emphasis must now be placed upon increasing soft-tissue tolerance of prosthetic materials now in use.

L.H.N.

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Estimating The Venous Pressure

The venous pressure has important significance. The veins originate at the capillaries and terminate in the heart. Their venous pressure has important bearing on the function of both the capillaries and the heart. The pressure in the smallest peripheral veins is a basis for deducing the minimal pressure in the capillary region, since the capillary pressure must exceed venous pressure. The effective venous pressure in the large intrathoracic veins reflects the diastolic filling pressure of the ventricles. Right atrial pressure ranges just above or below atmosphere pressure, but the pressure in the extrathoracid veins is 2-5 cm. of H_2O higher.

Exact measurements of the venous pressure requires insertion of a catheter into the right atrium. However, the venous pressure can often be estimated by simply observing the distension of the neck veins. For instance in the sitting position the neck veins are never distended in the normal person, because venous return from the head is conducted largely through the deeper cervical veins while the superficial veins are partially collapsed. However, when the right atrial pressure becomes increased to as much as 10 mm. Hg. the lower veins of the neck begin to protrude even when sitting. If right atrial pressure becomes more elevated to as high as 15 mm. Hg. essentially all the veins in the neck becomes greatly distended and the venous pulse becomes prominent in these veins. Such cervical venous distension is an important clinical sign usually indicative of congestive heart failure.

In estimating venous pressure one is really measuring the hydrostatic pressure. At the bedside it can very accurately be measured as the vertical distance between the venous pulse at the top of the column of venous blood in the neck veins and the reference point which is the angle of Louis (sternal angle). This can be felt as a transverse ridge formed by the angulation of the sternum at the articulation of the second rib. Long ago Sir Thomas Lewis[1] demonstrated that this angle between the manubrium and the body of the sternum bears a constant relation to the mean venous pressure with the patient in the supine, upright or any intermediate position. This relation reflects the relatively constant distance between the angle of Louis and the mid right atrium which is about 5 cm. of H_2O.

The point of venous pulsation used in estimating the height of the venous pressure is not the peak of the waves but the point near the end of diastole just before the carotid artery pulsation[2]. The normal venous pressure should not exceed 7 cm. H_2O which is 5.2 mm. Hg. This means 2 cm. above the sternal angle. With practice the venous pressure can readily be estimated at the bedside quite accurately. This method obviates the need for the routine measurement of venous pressure by direct puncture of an antecubital vein. No special equipment is necessary except a centimeter rule placed on Louis's angle perpendicularly and a pencil held horizontal to it at the level of the column of blood in the neck vein. Observations of the jugular venous pulse can then be made at frequent intervals[3].

Additional useful information may be obtained by noting the venous pressure response to abdominal compression—the hepato-jugular reflux[4]. This is performed with the patient comfortable and breathing quietly and gentle but firm compression applied over the abdomen. This will cause no significant increase of the venous pressure in the normal individual. However, if the venous pressure is increased by 2 cm. or more at the end of one minute of abdominal compression the patient may be assumed to have an abnormal increase in venous tone or an inappropriate response of the right ventricle to increased venous pressure, a common finding in heart failure as well as in constriction and restrictive heart disease.

There are certain limitations of estimating venous pressure in the neck. One obvious one is in superior vena cava obstruction or in the innominate veins which will cause bilateral or unilateral venous engorgement. Clinical estimation of venous pressure may also be misleading in the patient with shock because of marked veno-constriction, in pulmonary disease because of marked fluctuations of intra thoracic pressure and also in extreme obesity.

A patient with extreme elevations of venous pressure may have such distention that the pulsations may not be appreciated even with the patient sitting upright[5]. In this situation the neck often appears full and the venous pressure may be misinterpreted as being normal. It is only after the patient improves and the venous pressure decreases that the venous pulsations can be visualized. In the elderly patient the increase in venous pressure can usually be appreciated because the veins are often prominent. In the younger patient recognition may be difficult. When the neck veins are full observation of the veins under the tongue of the patient in the sitting or upright position may offer a clue to venous distention[6].

The pulsations observed in the neck veins may reflect not only the venous pressure but also other hemodynamic events of the heart. Tricuspid insufficiency which may be accoustically silent will reveal itself by a large pulsation in the jugular vein with each systole. Observations of the jugular pulsation can be particularly helpful at the bedside diagnosis of certain cardiac arrhythmias such a atrioventricular dissociation.

The examination of the venous pulsations of the neck is but one aspect of the cardiovascular physical examination and undue reliance of course should not be placed on any one physical sign. However, careful examination of the venous pulsation in the neck will reward the physician with the estimated venous pressure, furnish information regarding certain physiological events of the heart as well as evidence of cardiac arrhythmias.

L.H.N.

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Hypertensive Encephalopathy: A Medical Emergency

Hypertensive encephalopathy is the syndrome of sudden elevation of blood pressure, diminished central blood flow, central arteriolar constriction and cerebral edema. There then follows severe headache, convulsions, coma or a variety of transitory phenomena. The sudden appearance and disappearance of symptoms and bizarre neurologic picture, suggest that they may be due to focal or generalized cerebral ischemia. In fact equivalent symptoms can be produced by experimentally diminishing cerebral blood flow in animals and in man by temporary compression of the carotid arteries or as occurs in Stokes-Adams syndrome and in postural hypotension. Hypertension per se is not responsible since the syndrome can be produced without elevation of arterial pressure.

The common denominator of hypertensive encephalopathy and postural hypotension, the sine qua non of all the above conditions is a decreased cerebral blood flow. In the case of severe elevations of arterial pressure there is increased constriction of the peripheral arterioles, also found in the brain and retina. The highest recorded values of cerebral vascular resistance are in malignant hypertension and in hypertensive encephalopathy. The retinal vessels in eclampsia may be very narrow and become full again following effecive hypotensive therapy. In fact complete obliteration of retinal arteries can cause temporary blindness with vision restored as arteries become patent.

Cerebral edema is present in some cases of hypertensive encephalopathy. The spinal fluid pressure may rise to 400 mm. water and at autopsy the brain weight is increased 20-30 per cent, together with flattening of cerebral convolutions and reduction in size of the ventricles. The cause of the edema is speculative, but a rise in pressure in intracranial capillaries could accelerate filtration and therefore formation of edema.

The pediatrician faces this problem in patients with acute nephritis, the obstetrician, with toxemia of pregnancy and the internist in patients with hypertensive vascular disease. Fortunately the incidence of hypertensive encephalopathy particularly in eclampsia and that following chronic hypertensive disease has greatly decreased in the last decade during which diazide diuretics have become routine in the management of hypertension from whatever cause. Encephalopathy is always accompanied by an increased vascular resistance reflected in a high diastolic pressure. In anxiety states, the pressure is usually labile although it may be extreme. Arterial pressure may also be high in acute pulmonary edema but here carotid sinus pressure, sedation and digitalis can quickly lead to relief.

In hypertensive encephalopathy clinical experience has shown that clearing of the sensorium, cessation of convulsions, and reduction of vasoconstriction always follows reduction of blood pressure and the primary aim in treatment is to achieve quick reduction of arterial pressure. From the practical point of view the drug chosen to reduce blood pressure depends on the clinical condition of the patient particularly the degree of cerebral ischemia present. If the danger is not imminent and waiting one to two hours appears not harmful, intramuscular reserpine is the drug of choice. If, however, the patient is convulsing or on the verge of convulsions Finnerty[1] believes diazoxide becomes the drug of choice. There are advantages and disadvantages to these drugs that must be borne in mind.

With regard to reserpine the dose is 2.5 mg. intramuscular, the hypotensive effect is maximal in one to two hours. If salt retention is a factor as it is in eclampsia, then furosemide results in a prompt response. However, reserpine's action is delayed nasal congestion and increased tracheobronchial secretion can occur and even Parkinsonism if treatment is continued for 72 hours. Then there is the problem of potentiation by barbiturates and anesthetics leading to too great a drop in blood pressure at times requiring norepinephrine. Finally the problem of the infant delivered to mothers treated with this drug who must be kept on left side and their nasal congestion promptly corrected.

With regard to diazoxide Finnerty used 300 mg. i.v. rapidly in 15 seconds and if hypotension does not follow, he suggests dosage up to 5 mg. per kg. He reports its use in 314 patients and a drop of 35 per cent in mean arterial pressure within two minutes. The average duration of action is 10 hours and a complete clearance of the neurologic signs and absence of side effects occurred in 77 per cent of these patients. The fall in blood pressure was associated with increased cardiac output, dilatation of arterioles generally and increased cerebral blood flow. The benefit then is immediate onset of action maintenance of cardiac output, lack of signficant side effects, no drug resistance. These actions make diazoxide an extremely valuable agent for treatment of acute hypertensive encephalopathy.

However, because sodium retention can occur this can be overcome with pretreatment with furosemide 40-60 mg.[1] Transitory hyperglycemia can occur but this is easily prevented by pretreatment with tolbutamide[2]. Furthermore, if extravasation occurs, it is quite painful and requires temporary cessation locally and transfer to another site. These are simple technical problems, easily handled. With these in mind it appears the best treatment for hypertensive encephalopathy is diazoxide and furosemmide and since there occurs increased renal circulation as will with these drugs, they are obviously safe also for treatment of the hypertensive patient who also has impaired renal function.

L.H.N.

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The Control Of Serum Calcium Levels

Serum calcium is maintained with rigid physiologic levels. Ninety-nine per cent of calcium is present in the skeleton. The remaining one per cent is essential for the activity of a number of enzymatic systems including those responsible for the contractile properties of muscles and heart and for the transmission of nerve impulses. It is the concentration of calcium with appears to be critical in the extra-cellular fluids, particularly for the response of muscle, neural stimuli, and for the functioning of the blood clotting mechanism. The calcium of normal human plasma varies from 9-11 mg. per 100 ml. and exists in two major forms ionic calcium of 5-6 mg. per 100 ml. is the active form exerting its physiological effect, the second form of calcium is not diffusable and is bound to plasma albumin[1].

Our knowledge of the hormonal factors involved in calcium regulation has resulted from several recent advances in physiology and biochemistry. First was the purification of bovine parathyroid hormone (PTH) and partial characterization of its molecular features essential for its biologic activity. Direct measurements of PTH in serum by radioimmunoassay permitted a detailed investigation of the physiology of the parathyroid gland. It also led to examination of a variety of in-vitro and in-vivo models to define the mechanism of action of the hormone[2]. The last was the discovery of thyrocalcitonin (TCT) which has an action antagonistic to that of PTH[3].

PTH promotes mobilization of calcium from bones, increases tubular reabsorption of calcium and decreases tubular reabsorption of phosphate. It may have additional though relatively minor effects on the mammary gland and the gastrointestinal tract. The regulation of hormone secretion by the blood calcium level is the major factor responsible for the constancy of the serum calcium concentration in man. This can be shown by reducing serum calcium which at once increases PTH secretion and conversely by increasing serum calcium which at once stops it. These results have also been shown to occur by perfusing the parathyroid gland with high and low calcium concentrations which reveals that the control of calcium is at the level of the parathyroid cell. Hyperphosphatemia indirectly stimulates PTH by first lowering the calcium level in the serum.

The hormone is barely stored in the parathyroid gland. Since variation in secretion rate of the hormone can be detected within minutes after changes in the calcium concentration of the serum, it means that the hormone is continuously being synthesized. This has been confirmed by in-vitro studies in which explants of parathyroid tissue are exposed to different concentrations of calcium and the hormone production is assessed by the radioimmunoassay of the culture medium. From this method also has come the idea that the site of action of the calcium ion is the cell membrane itself.

The parathyroid can be rendered hyperplastic when chronic hypocalcemia exists. Clinical states of this type result from dietary inadequacy or poor calcium absorption secondary to the malabsorption syndrome or chronic renal disease. Hypocalcemia is also found in certain parturient animals. In all such situations a hyperplastic parathyroid results with a proportional increase in hormone secretion. Apparently the parathyroid glands adapt to chronic hypocalcemia by hyperplasia and an increase in the basal rate of hormone production. This type of increase in PTH production which can rise to 15-20 milli micrograms per ml. secondary to hypocalcemia is termed secondary hyperparathyroidism. In a few patients protracted stimulation of the gland of this kind may lead to a third state—tertiary hyperparathyroidism in which the glands become autonomous. Sherwood reports one such patient with severe renal disease in which in-vitro evaluation of the parathyroid tissue confirmed autonomy, that is it was no longer under calcium control.

When there is a parathyroid tumor the condition is termed primary parathyroidism. In such patients there is a correlation between the degree of clinical hyperparathyroidism—high serum calcium levels and the size of the adenoma. In such cases the elevated serum calcium does not shut off PTH production. In adenoma explants grown in tissue culture and hormone release evaluated by radioimmunoassay, showed no changes despite large variation in calcium concentration of the medium, a conclusive proof of autonomy.

PTH can also be produced by non-parathyroid tumors. Extracts of seven tumors, four lung, one adrenal, one parotid and one reticulum cell sarcoma produced a PTH-like substance in quantities varying between .75-8.90 mg. per gram. If the tumors are very large they could produce enough PTH even though the presence in each gram were low.

Most workers now accept the concept that PTH alone does not maintain the constancy of the serum calcium by a negative feed back mechanism but that another hormone now known to be derived from the thyroid gland—thyrocalcionin (TCT) tends to lower calcium levels in the serum[3]. The source of TCT in the thyroid is a special cell—parafollicular adjacent to the thyroid follicle. It is found in all vertebrates except cyclostomes. It may be secreted in times of calcium stress and may be more important in the development of the skeleton that in the stabilizing of serum calcium. Its physiologic significance in the adult is still a major question. In the absence of the thyroid there seems to be no difficulty in calcium balance. Furthemore the labile reservior of calcium in the skeleton and the minute to minute changes in PTH secretion in response to alterations in serum calcium seem adequate to explain the constancy of the serum calcium in man without the aid of TCT.

TCT may, however, have therapeutic indications even if it is of minor physiologic significance. For example it might assist in bringing serum calcium down in an acute hypercalcemic crisis. At present this is a medical emergency for which no completely satisfactory therapy exists. TCT inhibits reabsorption of calcium from bone and might reduce the accelerated turnover caused by a number of pathologic conditions, such as hypercalcemia, hyperphosphatemia and Vitamin D intoxiation. Its potential usefulness in osteoporosis is an important one that needs evaluation. The difficulty is that TCT seems to be less effective in the elderly and the hormone has not as yet been produced synthetically.

However, although parathyroid destruction renders a patient hypocalcemic, excess TCT could also result in hypocalcemia although no evidence for this type of hypocalcemia has yet been published. Mild hypocalcemia and tetany in one patient with a nodular goître disappeared after total thyroidectomy[4].

We have seen that disorders of calcium homeostasis occur when mobilization of the stable skeleton calcium reservoir is accelerated or when the secretion of PTH is excessive or diminished. Compensatory increase in TCT secretion are not sufficient to compensate for the autonomous function of parathyroid adenomas or hyperplasia or of ectopic tumors that produce PTH-like material.

L.H.N.

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Factors That Affect The Fertilizing Capacity Of Sperm

With the employment of sperm for artificial insemination both in animal husbandry and man, attention is being directed to the various factors that affect the fertilizing capacity of sperm. One is the effect of aging sperm both in the female genital tract and the male genital tract. Another is the problem of aging outside the body that might occur in the storage of sperm.

Aging of sperm apparently varies sharply with the environment in which sperm are held. Sperm retained in the male genital tract seem to retain their fertilizing capacity for long periods usually for several weeks in some mammals However, sperm do age in the male genital tract. Sperm became senescent in the distal epididymis and if there is a period of sexual rest the proportion of senescent sperm increases. In The rabbit aging sperm has been shown to produce death of the conceptus as well as a number of congenital defects[1]. Temperature also seems to be a critical factor in influencing aging of sperm, a higher temp in the testis and epididymis seems to age them faster than a lower one.

The period for which the sperm remains fertile in the female tract varies sharply with the species and often appears to be related to species peculiarities. Man and other primates occupy an unusual position in mammalian reproductive behavior regarding the possible aging of sperm in the female. Ovulation is spontaneous but there is no well defined period of sexual desire in the female and sperm may be deposited in the female tract at any time.

The survival period of human sperm in the female tract has usually been regarded as short of the order of 48 hours but the difficulties of precisely determining ovulation time make exact observation almost impossible. The rhythm method of birth control depends upon the belief that ovulation precedes the post-ovulatory temperature rise, but this is not a good indicator[2]. An important question that remains unanswered and is critical for the human subject is whether the fertilization of an ovum by a sperm aged by chance in the female tract or even in the male tract had deleterious effects. Such harmful effects have been observed so far only in Drosophilia and birds[3] for the female tract and in rabbits for aging of sperm in the male tract.

In recent years the ability to store sperm at low temperatures has come to be of great practical and economic importance in artificial insemination programs for farm animals[4]. There exist sharp species differences so that storage technics successful in one species are unsuccessful in others. In some species storage is limited to a few hours or days at temperatures near freezing. Various mediums appear to afford varying degrees of protection of the stored sperm. Egg yolk, milk and various electrolyte solutions have also been employed.

In several species including man, freezing of sperm is possible[5]. Bull semen can be readily stored for many months at −79°C. or at −196°C. Successful insemination with sperm stored for as long as ten years has been reported[6]. When frozen bull sperm is rewarmed about 50 per cent appear viable and normal offspring usually result from such sperm. The remaining viable sperm do not appear to have suffered damage that was sufficient to disrupt the genetic information they carry.

Human sperm is the most easily preserved by freezing. It requires no diluters or extenders to protect it and is relatively unsusceptible to cold shock. Jahnel[7] long before the protective action of glycerol and now dimethylsulfoxide was known has reported that human sperm recovered motility after cooling to as low as −269.5° C. and some cells survived for forty days at −79°C. Sherman in 1965[6] reported that twenty-four children in the U.S. and Japan have been born of frozen semen.

In view of the economic importance and widespread practice of artificial insemination it is surprising that studies of congenital defects among offspring of stored sperm have not been made. Some veterinarians, however, believe that this may reflect the fact that the apparent incidence of such defects among offspring surviving to term is so low as not to have been considered of economic importance. The theoretical and practical importance of such data becomes obvious when it is realized that banks of human sperm are coming to be considered seriously and that present technology is apparently adequate at least for the beginning of

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such a program. The ambiguous legal status of children born of artificial insemination is currently under review in several states and in 1967 the Oklahoma Legislature passed legislation assuring the legal status of children born of artificial insemination. Of course, when sperm are used decades after the donors have passed away no such legal entanglements may be expected[3]

L.H.N.

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Bephenium Hydroxynaphthoate (Alcopara)

Bephenium hydroxynaphthoate (Alcopara—Burroughs Wellcome), an anthelmintic drug, is new to the United States but has been used in other countries for nearly 10 years, primarily for the treatment of hookworm infections. It is also moderately effective against Ascaris, but less so than Piperazine Citrate USP (Antepar; and other brands), and the manufacturer recommends it for the treatment of Ascaris only when it occurs concomitantly with hookworm infection. Nausea, vomiting, and diarrhea are the only frequent side effects of bephenium.

HOOKWORM—Two species of hookworm infect man—Ancylostoma duodenale ("old-world" hookworm) and Necator americanus ("new-world" hookworm). Most of the studies showing favorable results with bephenium have come from Egypt, where Ancylostoma duodenale infections are frequent. These studies indicate that the drug is effective against Ancylostoma in up to 95 per cent of patients, with either a single oral dose of 5 Gm (2.5 Gm bephenium base) or two doses of 5 Gm each, given in a single day; the manufacturer recommends the two-dose regimen.

Several studies have shown that bephenium is less effective against Necator. A single oral dose of 0.12 ml/kg, with a maximum of 5 ml, of Tetrachloroethylene USP is superior. Tetrachloroethylene is available in many places only as a veterinary drug, but capsules for human use are available from Lustgarten Labs., Philadelphia, Pa. Bephenium is, however, the best alternative to tetrachloroethylene; the adult dose is 5 Gm twice a day for three days. For children weighing under 50 pounds, one-half the adult dose is recommended.

ASCARIS—Using two 5-Gm doses of bephenium in a single day, H. C. Hsieh et al. (Amer. J. Trop. Med., 9:496, 1960) reported a 65 per cent cure rate in patients with Ascaris infection. Other workers have obtained similar results. Thiabendazole (Mintezol) is very effective against Ascaris, but piperazine (1 to 3.5 Gm once daily for two days) continues as the drug of choice, at least until there has been longer experience with thiabendazole (Medical Letter, Vol. 9, p. 99, 1967). Tetrachloroethylene is ineffective in Ascaris infection.

ADMINISTRATION—The granules of bephenium are mixed with water or, to make a more palatable preparation, milk, chocolate drink, orange juice, or a carbonated beverage. No other food should be given for two hours.

CONCLUSION—For Ancylostoma, bephenium is the drug of choice and is highly effective. For Necator, tetrachloroethylene is more likely to be effective. In Ascaris infection, piperazine is the drug of choice, with thiabendazole the recommended alternative. In patients with combined hookworm and Ascaris infection, it may be preferable to treat the Ascaris with piperazine and then to treat the Ancylostoma infection with bephenium, or Necator with tetrachloroethylene.

Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N.Y., Vol. 10, No. 15 7/26/68

Common Complications of Surgery on the Cervical Spine

James A. Albright, M.D., Stevenson Flanigan, M.D., and
Wayne O. Southwick, M.D.

The purpose of this report is to point out the principal complications encountered during surgery of the spine. The problems seen in the treatment of patients with spinal cord compression and those resulting from anterior fusion of the vertebral bodies will be considered primarily. Indications for these procedures are dealt with elsewhere.[1] [2] The discussion will focus upon the cervical spine primarily and attention is directed to those complications which in our opinion, are the most important and are unique to surgery in this area.

While many patients requiring surgery on the cervical spine can be handled adequately by a single specialist, close cooperation between the Departments of Neurosurgery and Orthopaedic Surgery is essential for maximum benefit to the patient, particularly for more serious problems, such as spinal cord compression. The most expert opinion available should be utilized and treatment administered accordingly. With this philosophy, additional forms of treatment will be available for use. Might not the greatest complication be failure to initiate that form of treatment which would enhance functional recovery?

Our surgical experience in the past eight years includes a total of 65 cases with spinal cord compression of which 35 involved the cervical spine, and 48 anterior cervical spine fusions, plus an equivalent number of cases in other categories (simple fusions, tumors, etc.).

The majority of patients with disease of the cervical spine are in jeopardy of paralysis (or increased paralysis) because of injudicious handling from professional, as well as non-professional, personnel. Every motion, every examination, and every treatment is a threat to the patient who depends completely on others for his care. Although the list of potential dangers is infinite, injury is more likely to occur from hyperextension of the neck for myelography or for intubation, failure to maintain alignment of the head and neck in simple movement of the patient, and the technical effort for roentgenographic excellence in an unstable spine.

TRACTION: Skeletal traction is undoubtedly one of the most important adjuncts in the management of the broken neck. When there is any question of stability, it is far safer to treat the patient as if the spine were unstable. The surgeon must be familiar with the proper technique of inserting skull tongs.[3] [9] Most important in the use of tongs is the location, method and depth of insertion. There are many types available but in all types the points should penetrate the outer cortex of the skull, but not the inner. Brain and epidural abscesses have been reported from excessive skull penetration, and we have seen examples of each. The initial hole should be drilled using the proper guide (the exact type of guide depends on the type of tongs used), rather than an ordinary drill bit, since the purchase is greater when the tongs fit the drill hole exactly. If the tongs are well-seated and kept from loosening, it is rare they will penetrate the inner cortex or fall out of the skull. Usually the line of insertion should be across the vertex on a plane extending from the center of the neck up through the external auditory meati. (figure 1). If some flexion or extension of the neck is desired, the point of insertion can be slightly anterior or posterior to the neutral position, or the traction can be adjusted to pull anterior or posterior to the line of the body. Extreme caution must be used when determining the proper direction of traction (if this varies from neutral) since an im-

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Supported in part by Public Health Service grant T1 AM 5416-04.

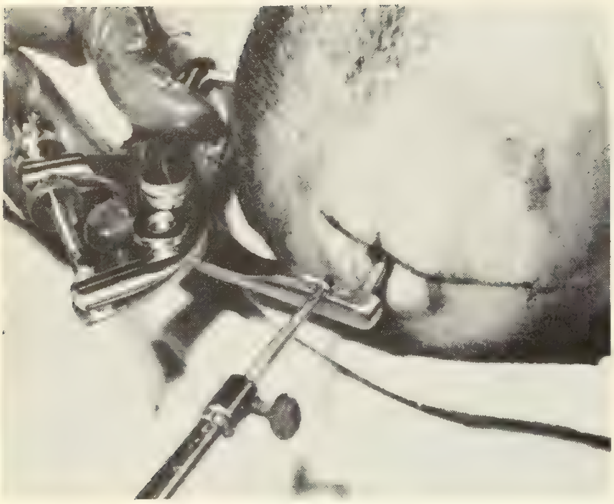

Figure 1

Insertion of Crutchfield tongs: A transverse line is drawn in line with tip of mastoids. After making a stabwound the tongs are held in the desired position to obtain proper angle for drill hole.

proper pull may increase the pressure on the spinal cord. One patient, who was referred to us following an injury, had almost complete quardriplegia which had been induced from imporper traction. In this patient the tongs were positioned unusually far forward, which we thought produced additional compression of the spinal cord and was the contributing factor to the increase in symptoms.

Since traction provides relative, but by no means absolute, stability, the patient must be handled with extreme care to avoid repeated insults to the spinal cord. If transient symptoms (particularly pain) occur with movement of the head or when the patient is turned, or if a patient with quadriparesis is not improving, it is advisable to reinforce stabilization with sandbags to either side of the head and to consider surgical stabilization.

Surgery (Surgical Complications)

ANESTHESIA: Proper anesthesia is vital for safe spinal surgery and the choice will vary with the capability and experience of the anesthesiologist. Local anesthesia with the support of an anesthesiologist is the safest for the patient, but if a long procedure is anticipated it can be difficult for surgeon and patient alike. The patient can become very uncomfortable and restless from lying in one position, and the quality of the procedure may be compromised if the surgeon's attention is diverted from the surgical procedure. Local anesthesia should be used if the spine is grossly unstable. It has been quite satisfactory for a simple laminectomy, fusion, or re-exploration in the cooperative patient.

General anesthesia can be satisfactory for most procedures, if nasotracheal intubation is used and the tube inserted with the patient awake. Spinal cord compression could result from manipulation of the neck during insertion of the tracheal tube, although we have never seen this complication.

LEVEL OF SURGERY: That surgery should be performed at the level of the pathology is obvious. We have treated three patients who had been operated upon at the wrong level. In each patient this error resulted in an inadequate exposure of the pathological process. None of the three had had an x-ray taken during the procedure, and in two of the cases the error was not recognized until reviewed for our study. We usually obtain an orientation film during surgery, and this has been effective in avoiding this complication.

SURGICAL APPROACH: The particular surgical approach used varies with the surgeon and is often not crucial. Unless rigid internal fixation is planned, it is generally preferable to not remove remaining supporting elements unless absolutely necessary.[4] (Figure 2A & B) This is vitally important when there is tumor or infection in the verte-

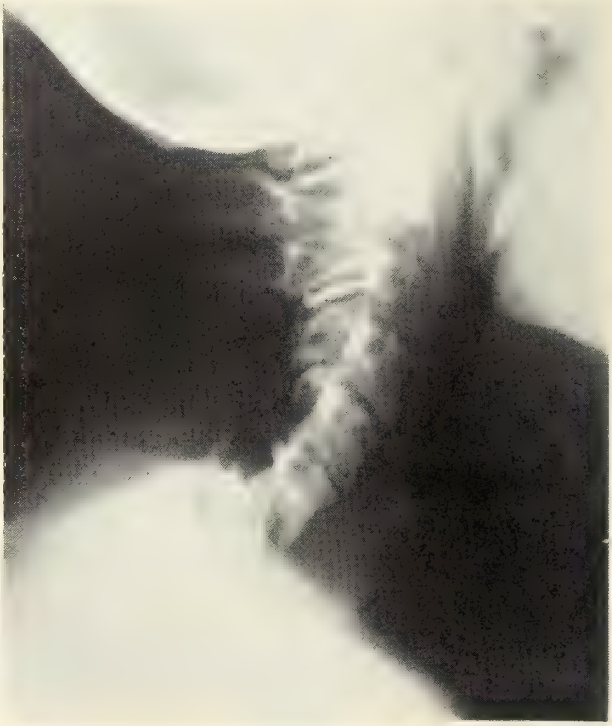

Figure 2A

This 52-year-old woman had previously had a laminectomy because of radicular pain. Since the spine began to subluxate following surgery, an anterior fusion was attempted, but resulted in further subluxation. Fortunately, there was no evidence of cord compression.

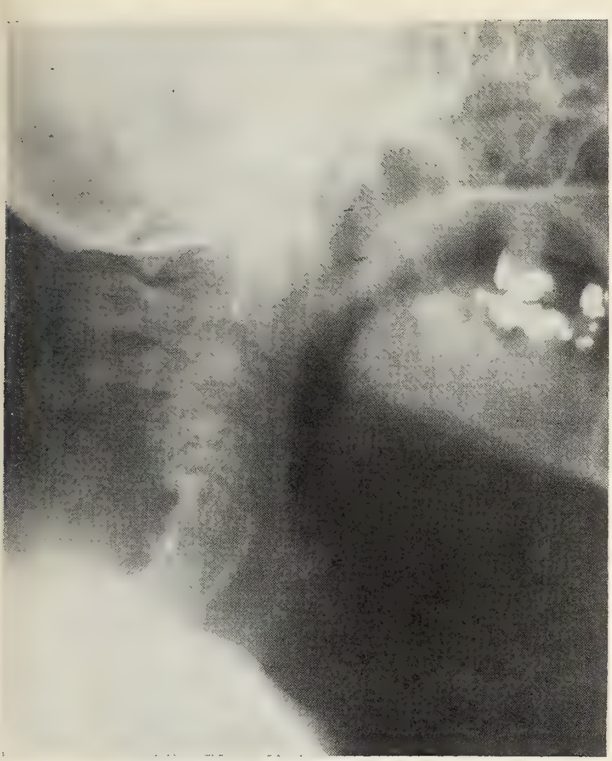

Figure 2B

Following reduction with traction a second attempt at anterior fusion was successful.

bral bodies. In such conditions, decompression of the cord should be performed by the posterior route only if the pathologic process is posterior. Anterior decompression can be equally effective and preserves the posterior structural anatomy. When the disease involves the vertebral body, attempts at decompression by laminectomy not only does not allow for either adequate decompression or adequate exposure, but it can produce severe and fatal instability by weakening the only remaining stabilizing elements.

CASE REPORT: R. J., A 47 year old white female was admitted on August 31, 1965, with severe quadriparesis. She had a past history of mild low back pain and neck stiffness for 15-20 years. For 7-8 years she had had osteopathic manipulations of her neck, which for a two year period had been given regularly every one to two weeks. (Figure 3A & 3B). There was a history of numerous apical abscesses in her teeth. Two years prior to admission she had developed pain in the upper extremities and for one and a half years had had signs of long tract involvement in both the upper and lower extremities. Because of increased difficulty in walking, a myelogram had been performed in May 1965, (Figure 3C), and had been followed by increased weakness and incontinence. One week later she had had a laminectomy following which she had developed a progressive increase of the quadriplegia to almost complete loss. (Figure 3D). At the time of admission neurological function had improved somewhat, especially in the upper extremities, but she was completely dependent in all activities. The white blood cell count was 7,700. On September 2, 1965, bone biopsies at C4, C5 and C6 levels, through an anterior approach, grew anaerobic diptheroids, and showed postitive cocci on smear (but not culture). The biopsy was consistent with osteomyelitis microscopically. A subsequent biopsy and culture at L 3-4 interspace (because of loss of disk space and sclerosis) grew out staphylococcus aureus and she was started on appropriate antibiotics. In December 1965 a facet fusion of C 3-6 was performed because of instability of the spine and neurologic deterioration, (Figure 3E). Following fusion she developed increased quadriparesis and was re-explored immediately under local anesthesia. A hematoma was found and when it was evacuated she was almost completely relieved of symptoms immediately. Eleven months following fusion her function was markedly better than it had been prior to fusion and she was still improving. She was continent, was independent in activities (although not normal in strength), and had normal sensation at rest, but complained of parethesias in her hands when active.

This case demonstrates several complications which can occur during treatment of patients with cervical spine disease. It is obvious that an accurate diagnosis is mandatory for the institution of proper therapy and when there is any question of infection or tumor a biopsy should be performed. In our hands open biopsy is more satisfactory than needle biopsy. The inadvisability of using manipulations

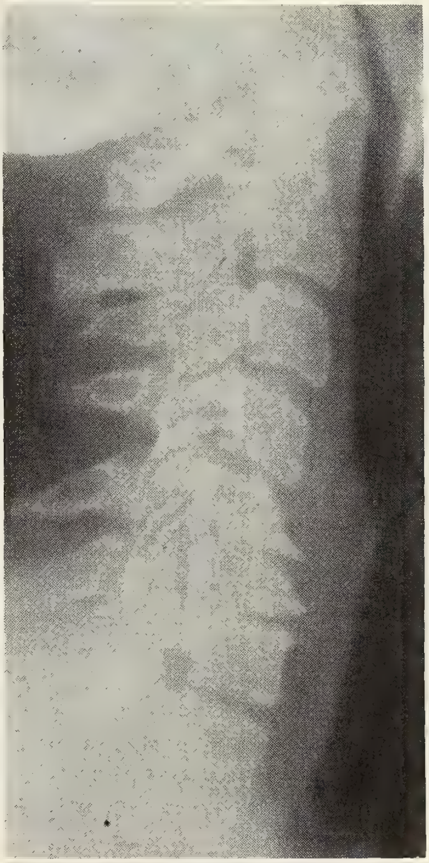

Figure 3A

Six years prior to admission.

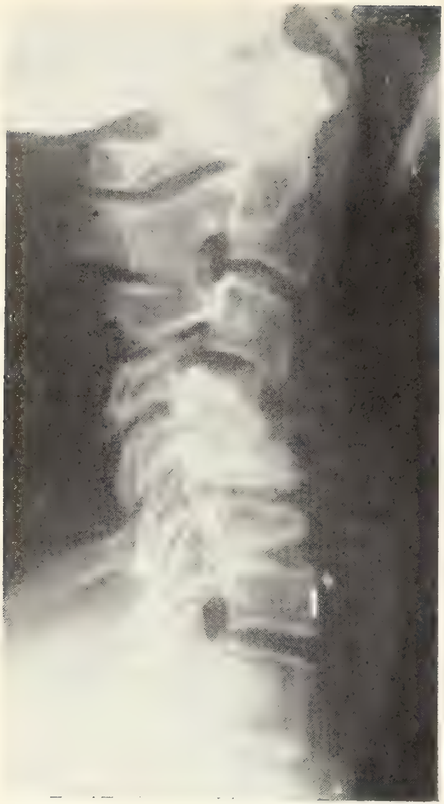

Figure 3B

After onset of mild long tract signs (immediately prior to myelogram). Severe destructive changes of C4, 5 and 6 with destruction of the C4-5 disk space and merging bodies.

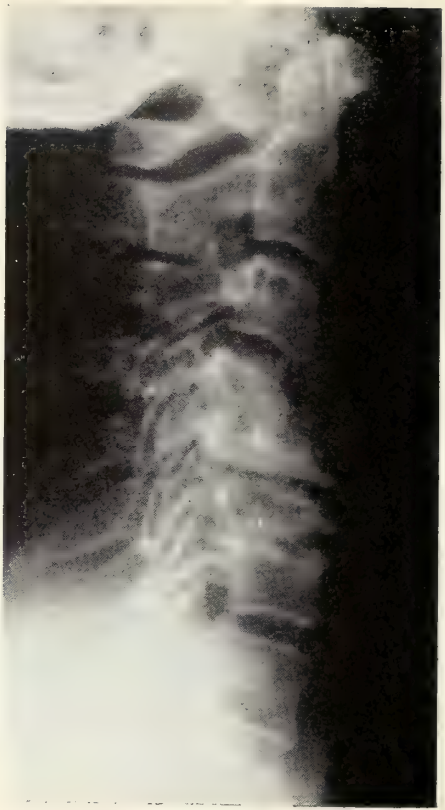

Figure 3D

Laminectomy one week after myelogram, was followed by almost complete loss of function.

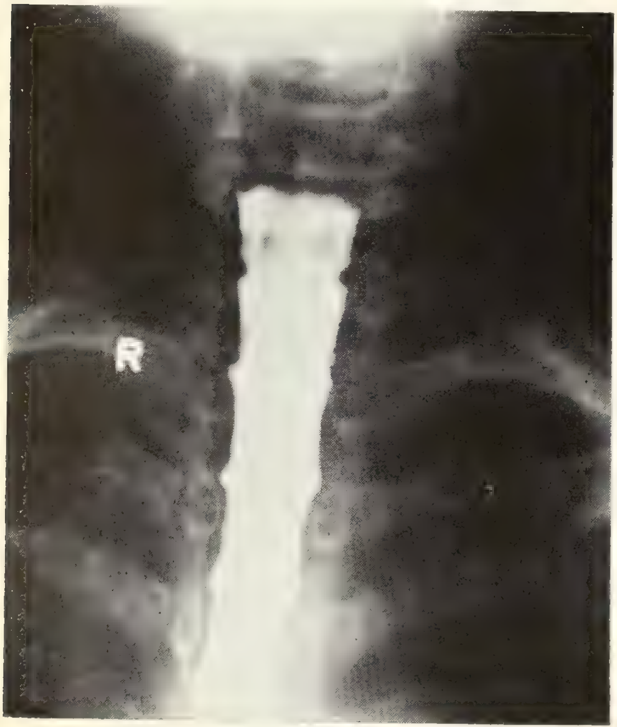

Figure 3C

Myelogram demonstrating a block. Symptoms increased somewhat concomittant with myelogram.

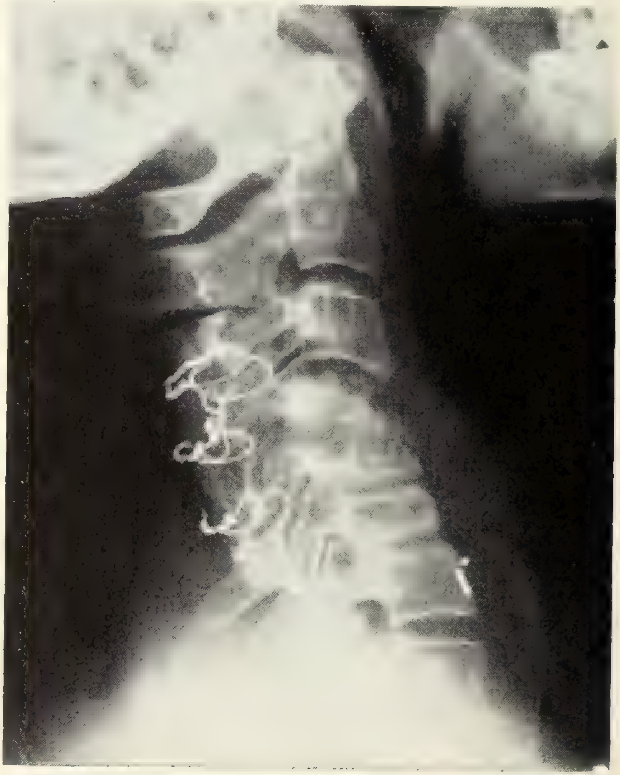

Figure 3E

Following facet fusion.

for symptomatic treatment of degenerative disk disease is illustrated. In this patient the diseased spine probably did not benefit from the manipulations, and may have been aggravated by the prolonged course of treatment. It is known that an increase of symptoms may follow a myelogram, and in our series two patients had this complication. The probable mechanism involves extension of the spine which causes the ligamentum flavum to bulge into the spinal canal, reducing the internal anterior-posterior diameter. When a spur or a bulging disk is present anteriorly in the spinal canal, the spinal cord may be compressed between the anterior element and the buckled ligamentum flavum when the neck is extended.[5] The most crucial decision in the case presented was that of the approach for decompressing a spine which was already unstable from severe disease in the vertebral bodies; and unfortunately, the method selected involved laminectomy without providing for stabilization. This approach did not expose the disease and further weakened the spine, so that the resulting outcome might well have been anticipated.

We have had four patients with infection of the vertebral body referred to us after laminectomy. Three of these patients had been made significantly worse by surgery and one had not improved. The anterior approach would have prevented these complications. In the dorsal or lumbar spine either an anterior, an anterior-lateral or posterior-lateral approach may be used.

We have performed three anterior decompressions for paraplegia (secondary to infection in two patients and tumor in one patient). Two of these patients showed improvement, and the one who did not improve had had a previous laminectomy. We have used this approach for biopsy or decompression of the vertebral body in 36 patients who have not had paraplegia and have had no serious residual complications from the surgery.

SURGICAL TECHNIQUE: When a spinal fusion is performed in a patient who has had a previous laminectomy, only large pieces of bone should be used and these should be securely fastened to adjacent fixed bony elements, since loose pieces of bone cannot be controlled and may lodge against the dura causing cord pressure. We prefer to wire the grafts to the facets, (Figure 4), which provides immediate fixation, leaves no loose fragments in the wound, and the canal remains unroofed and decompressed.

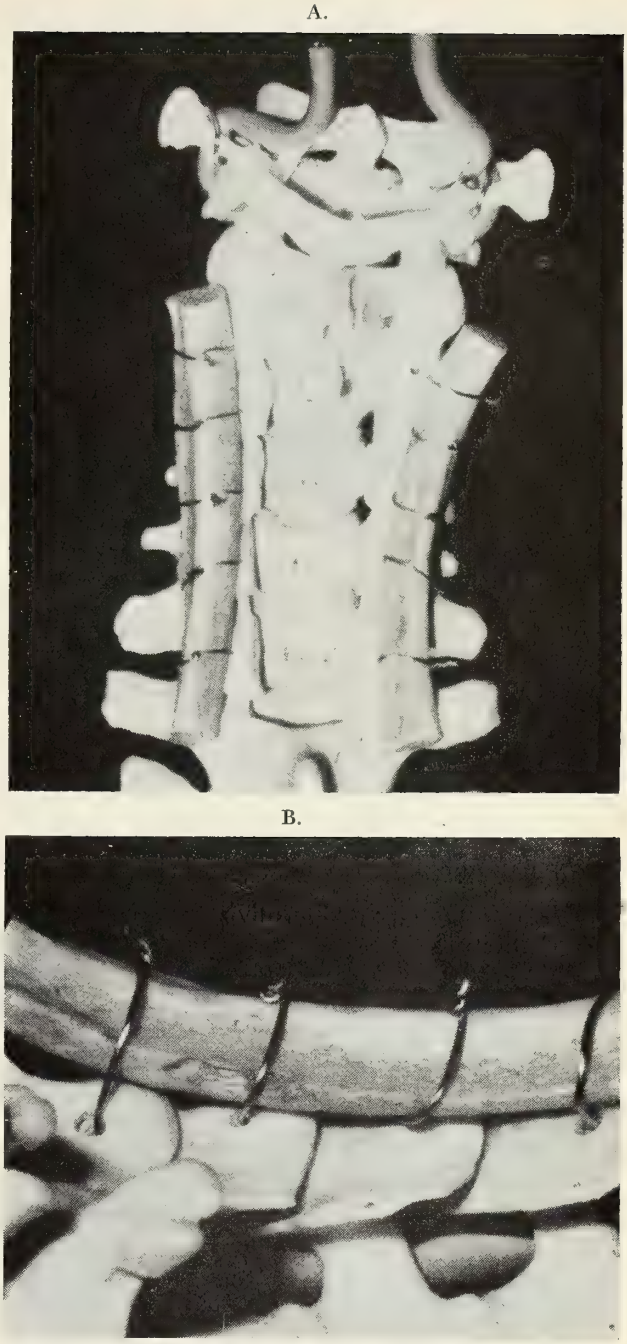

Figure 4

A and B. Facet fusion. Grafts are held with wire passed thru the inferior facets and out thru the facet joints.

Persistent symptoms from the donor site are not uncommon,[6] and these usually reflect the degree of concern generally given to this portion of the procedure. It is distressing to obtain a good result from the spine surgery itself, and then be confronted with symptoms arising from the donor site. Chronic symptoms include pain, which may be due to nerve entrapment, or less commonly, a mass as seen in Figure 5. Donor site symptoms can, of course, be

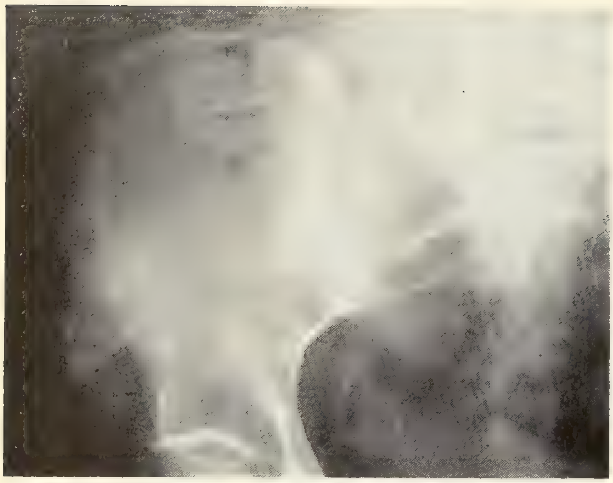

Figure 5

New bone formation at donor site. Excision was required because of symptoms.

obviated by the use of homogenous or heterogenous bone, but we are not yet convinced that the results are equal to those obtained using autogenous bone.

An infrequent, but dramatic, complication is a perforation of the dura. If the cord has not been injured also, this is a relatively benign problem, although the defect in the dura should be closed.

Post-Operative

INCREASING PARALYSIS: Any significant increase in paralysis following surgery is an emergency which demands re-exploration. During re-exploration the cause can usually be discovered and relieved with the expectation of clinical improvement to the pre-operative level. In our experience there is no basis for the opinion that increased paralysis is due to non-specific trauma resulting from a long and difficult surgical procedure; rather we have found that increased symptoms result from a specific insult to the spinal cord and should be treated as such.

Five of our patients have had a significant increase in symptoms following a surgical procedure and were re-explored. In three of these a hematoma was found, in the fourth an improperly wired bone graft had displaced and in the fifth an H-graft had fractured and angulated. The three patients with hematomas were completely relieved and the other two patients improved significantly, but not completely. Two patients, referred to us after treatment elsewhere, had had a marked increase in symptoms and had not been re-explored. One of these had no recovery and the other had poor return.

At the time of re-exploration the cause of the worsening neurological condition has been obvious, and in two of our patients done under local anesthesia, the improvement was dramatic at the operating table, (demonstrated by the first case report).

Problems Following Anterior Fusion

An anterior cervical spine fusion is an excellent procedure in a patient with the proper indications assuming technically competent surgery is performed. Symptoms are often dramatically improved or completely gone immediately following surgery. The operation demands meticulous attention to detail, particularly clearing the interspace of disk material (especially posteriorly and posterior-laterally), shaping the graft to fit perfectly, and providing stability to the graft. In 48 consecutive cases of anterior fusion the most significant complications we have encountered have been:

1.) *Malunion:* Impaction of the graft into the vertebral body with subsequent angulation of the spine at that level can occur if one or both of the subchondral cortical plates has been removed. This complication is particularly common following the dowel-type of fusion.[7] (Figure 6) It can be prevented by using the Robinson fusion. This requires careful removal of all the disk material, careful preservation of the cortical plates, and insertion of an

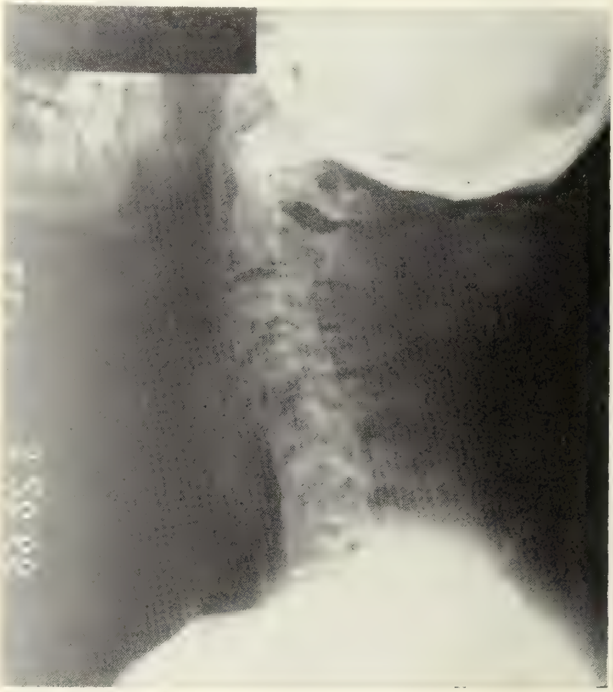

Figure 6

Angulation after interbody fusion using dowel technique. (The final result in Case F.S.)

iliac graft with the cortex of the bone graft aligned perpendicular to the plane of the interspace. Once this complication has occurred and residual deformity is present, treatment of the reversed angulation which results is extremely difficult and is not usually advisable. If symptoms warrant, a simple posterior spine fusion was often satisfactory in Keblish and Keggi's series.[7]

2.) *Spinal Cord Injury:* One patient developed a cordotomy effect from direct trauma to the spinal cord at the time of re-operation. Spinal cord injury is possible during any type of surgery of the spine, but is described here since it occurred during an anterior fusion.

CASE REPORT: F. S., A 60 year old male with mild diabetes was admitted initially for a cervical laminectomy of C5 on the left because of pain in the left upper extremity. Following surgery the symptoms were relieved for awhile, but neck pain recurred radiating into the right upper extremity with absence of the triceps jerk bilaterally. Therefore, he was readmitted for an anterior dowel-type fusion of the C 5-6 and C 6-7 interspaces which produced transient relief. However, the symptoms recurred and x-rays of the cervical spine demonstrated an extrusion of the anterior cortex of the bone graft from the C 5-6 interspace, plus a reversal of the normal lordotic curve. At re-operation some additional disk material was encountered at the C 5-6 interspace on the right in the region of the Joint of Luschka, and when removing it a cerbrospinal fluid leak was produced associated with inadvertant trauma to the spinal cord. Postoperatively, there was continued pain in the right upper extremity with additional findings including increased loss of the right C-6 nerve root, a Horner's syndrome on the right, and findings of injury to the right lateral spinal thalamic tract (loss of pin prick and temperature sensation on the left below T-1). A subsequent myelogram showed defects at the fourth and fifth cervical interspaces on the right. The spinal fluid protein was 68 mg percent. Fusion occurred at the operated levels but the angulation persisted. (Figure 6)

Fortunately the result in this case was not a catastrophe, but it emphasizes the potential hazard of an inadvertant motion during surgery. Although faulty technique must be condemned, errors continue to occur during surgery (more frequently than admitted usually). Although each error does not cause harm to the patient, the possibility of permanent impairment exists constantly and must be balanced against the benefits to be gained when considering surgery initially. This is perhaps the largest variable in any surgical procedure, and is difficult to determine since the degree of manual dexterity and judgement varies with each surgeon.

3.) *Extrusion of Graft:* We have seen the graft extrude in four cases, (Figure 7). It usually results either from improper seating of the graft or from use of a graft of insufficient height which allows motion to occur in the interspace. If the motion is great enough, the graft may eventually be extruded. Extrusion may occur spontaneously with no history of any precipitating incident, but frequently the onset can be traced to a traumatic event which may be severe, such as an auto accident or a fall, or it may be no greater than a cough. It is for this reason we feel that some form of post-operative support is advisable, although generally we prescribe nothing greater than a collar which provides minimal or no actual support but does remind the patient to limit his activities. When the graft extrudes, symptoms may recur, or new symptoms, such as dysphagia, may appear. In most cases re-exploration is indicated.

4.) *Horner's Syndrome:* This may result from trauma to the sympathetic nerves and is usually secondary to retraction. The symptoms are usually temporary and in our series there has not been a case in which it has been permanent.

5.) *Discitis:* Two of our cases developed "discitis" in an interspace which had not been surgically attacked, but had been injected with dye for x-rays at the time of surgery, (Figure 8). We have not found evidence of infection, and speculate that changes may be related to an inflamatory response

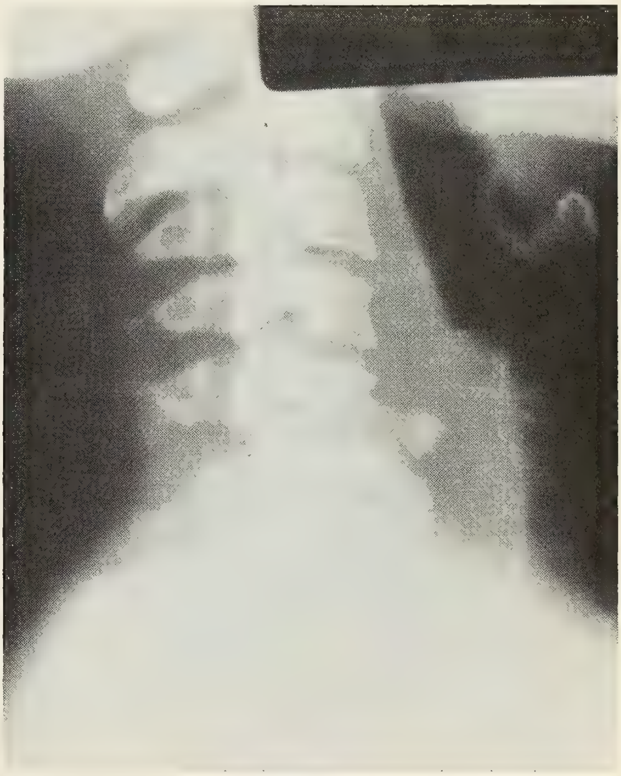

Figure 7
Extrusion of graft (the graft had not been properly seated).

following injection of dye into a relatively avascular interspace. Both of these patients have required a subsequent fusion of the involved interspace because of pain. We no longer obtain routine discograms at surgery because of this complication and because we have found that interpretation is difficult. We presently rely more upon a pre-operative myelogram.

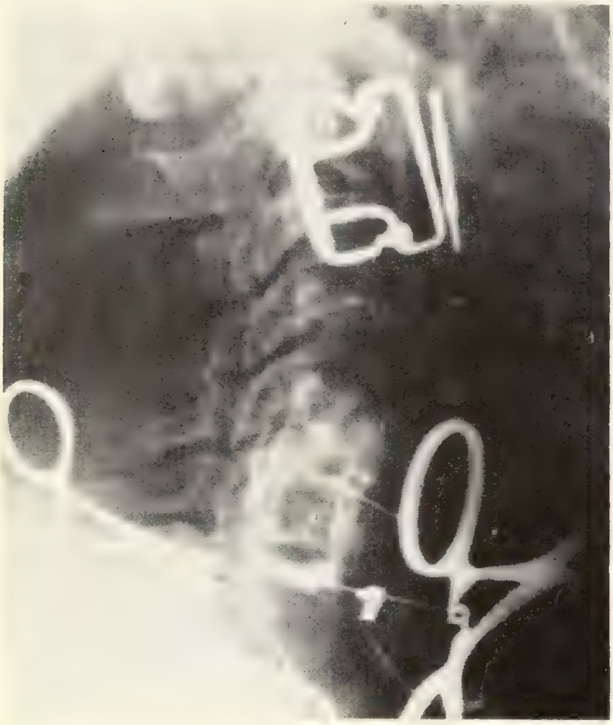

Figure 8A
Discograms of C 5-6 and 6-7 done at time of surgery.

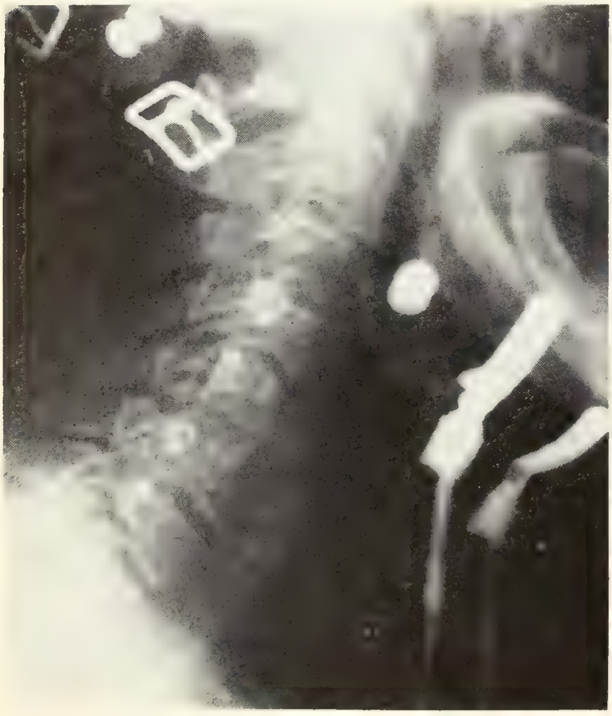

Figure 8B
Immediately after interbody fusion of C 5-6. The C 6-7 interspace was not disturbed at surgery except for the discogram.

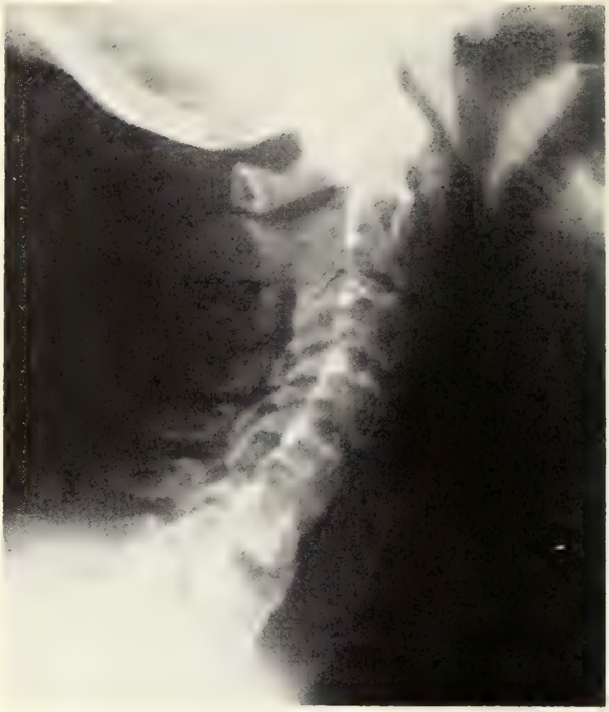

Figure 8C
Six months later. Fusion of C 5-6. "Discitis" at C 6-7. surgical fusion of the C 6-7 interspace was performed later and symptoms (pain) cleared.

There are several other significant complications which are uncommon, but of which we have seen cases.

6.) *Injury of Laryngeal Nerves:* Permanent changes in the voice can occur and are either secondary to injury of the recurrent laryngeal nerve which affects the vocal cords, or secondary to injury of the superior laryngeal nerve which affects the pharyngeal and cricothyroid muscles and sensation in the larynx. The latter nerve usually crosses the upper part of the operative field in close proximity to the superior laryngeal artery and may be divided into several small filaments, which should be judiciously preserved. If the superior laryngeal nerve is injured, the change in the voice is not as dramatic as when a vocal cord is paralyzed, but the pitch will be lower, the voice will be less clear, and sensation in the larynx will be impaired, which may cause dysphagia.

Injury to the recurrent laryngeal nerve is a well-known complication of paratracheal surgery but fortunately is uncommon. Anatomically, the nerve is medial to the plane of dissection and is not in great jeopardy. Since transient paralysis is due to excessive retraction, exposure from the left is safer theoretically than from the right, because the nerve on the left has a longer course and lies deeper, in a less exposed position, as it ascends along the esophagus.

7.) *Perforation of the Esophagus:* This may result either from injudicious dissection or retraction, and is an extremely serious problem. We have knowledge of two cases, of which one expired because of his complication, and the other was critically ill, but survived.

8.) *Injury of Vertebral Artery:* Finally, perforation of the vertebral artery is potentially possible if dissection is carried too far laterally. It has been reported,[8] but fortunately is rare.

Summary

Several complications seen during surgery on the cervical spine have been described. Particular emphasis has been given to the surgical approach for tumors or infections of the vertebral body and to the treatment of increased paralysis following surgery.

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The saddest thing about old age is that its future is behind it.

Ramon y Cajal

The Umbrella Pack to Control Pelvic Hemorrhage

R. Clay Burchell, M.D.

Pelvic hemorrhage is a serious gynecologic problem. Every clinician can remember a time when bleeding threatened a patient's life. Indeed, the commonest remark made at a recent exhibit[1] of the umbrella pack was: "I wish I had known about this last year"! This ingenious pack practically insures the clinician that he can control pelvic hemorrhage.

The umbrella pack was described by Logothetopulos in 1926.[2] Undoubtedly, he was inspired by the Mikulicz drain. Logothetopulos believed the pack would absolutely stop pelvic bleeding. To demonstrate this he performed hysterectomy without ligating vessels and inserted the pack. *There was no bleeding!* This bold demonstration attracted attention and resulted in widespread use of the pack in Europe. However, it is little known and seldom used in this country.

The name "umbrella pack" was coined by residents at Research and Educational Hospitals of the University of Illinois. They found nurses knew what they wanted when they asked for an umbrella pack but were confused when they asked for a "Logothetopulos tampon". The new name was adopted only for the sake of simplicity.

The umbrella pack is composed of a square cloth of nylon or cotton about 24 inches to a side. Fifteen to 20 yards of 2 inch gauze is placed into the center of the cloth. A funnel-shaped sling is then formed when the 4 corners of the cloth are brought together. The pack, therefore, has a bolus of gauze inside the cloth at one end and a tail at the other end (the 4 corners of the cloth). The bolus of gauze is placed in the true pelvis (not the uterus) with the tail coming out through the vagina. Traction on the tail pulls the bolus of gauze snugly into the pelvis so that bleeding points are compressed Figure 1. Pressure on bleeding points is controlled by the amount of traction and by the amount of gauze. As demonstrated by Logothetopulos, compression can be increased enough to stop major arterial bleeding.

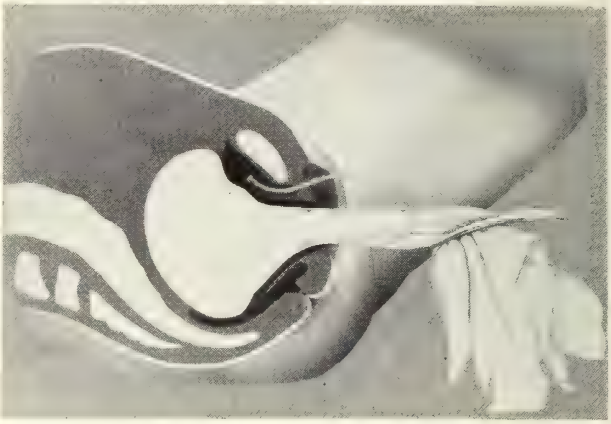
Figure 1. Traction on the tail of the umbrella pack compresses bleeding points.

Inserting the Pack

The pack can be employed with either abdominal or vaginal operations. However, a different technic is used to insert the pack with each type of operation. Abdominally, the pack is *formed outside the pelvis* and inserted intact by having an assistant pass a uterine dressing forceps up through the vagina and grasp the tail Figure 2. The bolus of gauze in the pack seats itself according to pelvic contours as the tail is pulled out through the vagina by the assistant.

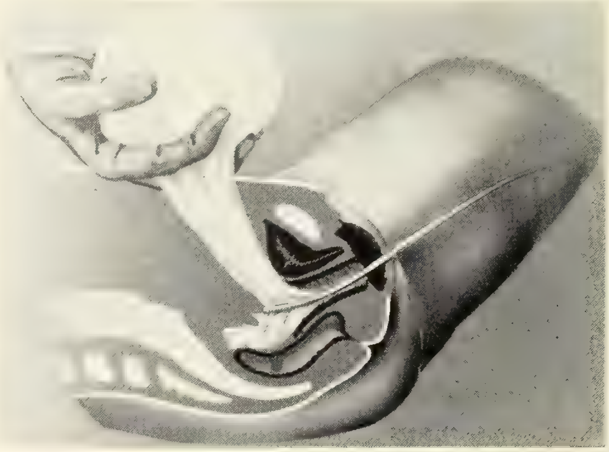
Figure 2. The tail of the pack is pulled down through the vagina.

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For vaginal application, the pack is actually *formed inside the pelvis* Figure 3. The square of nylon is held up in front of the vulva by the corners and the center is pushed through the vagina into the pelvis. Sufficient material is pushed in to enclose about 15 yards of gauze. Gauze is then packed inside with a ring forceps. The 4 corners are brought together and pulled down to seat the pack.

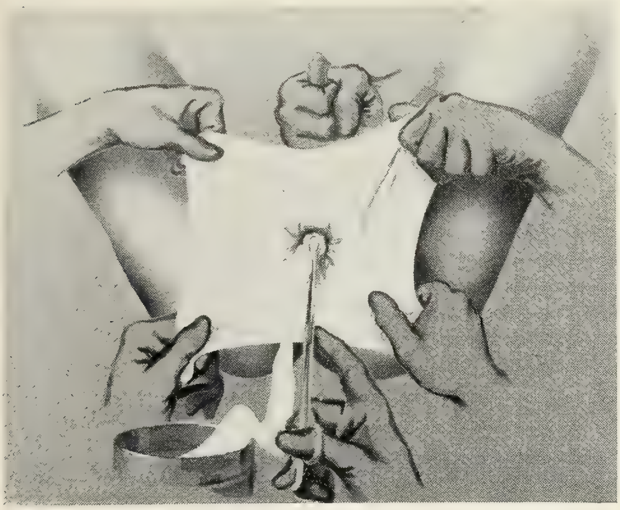
Figure 3. Gauze is packed inside the nylon cloth.

The pack is always removed vaginally irrespective of how it was inserted. The end of gauze put in last is grasped and pulled out. The nylon cloth is easily removed after all the gauze has been pulled out. Removal of the umbrella pack is less painful and simpler than when gauze alone is used. The outer nylon cloth prevents adhesions between gauze and bowel.

Materials for the pack are available in any operating room. At first, we cut up old cotton sheets but found that considerable amounts of material bunched up when the 4 corners were brought together to make a tail. Also, difficulty was encountered in pulling the tail through the vaginal apex. Lubricating jelly on the outside of the pack helped to some extent. However, the problem was not solved until nylon (Owen's non-adherent surgical fabric) was used. It was less bulky and could be easily inserted.

The pack should be firm, plain gauze is preferable to an elastic or compressible type. The amount of gauze employed depends upon where the bleeding point is. From experience we found the true pelvis is pretty well filled by a pack containing 15 yards of gauze. If the bleeding point to be compressed is near the pelvic brim, 20 yards might be necessary. We used 25 yards in one patient with total exenteration to control bleeding. An oversized pack was made up and forced into the pelvis to produce lateral pressure against the sacrum.

Clinical Use

The umbrella pack has been employed eight times in critical situations after other methods (including internal iliac artery ligation in four patients) had failed to achieve hemostasis. Bleeding was quickly and effectively stopped. Seven patients recovered. One, a patient with total exenteration, died from bleeding stress ulcers on the 8th postoperative day.

Hemorrhage was secondary to operation in all the patients. Bleeding arose from various sites: large raw surfaces associated with hematoma or pelvic inflammatory disease (5 patients), sarcoma growing into the pelvic wall, the sacrum during total exenteration, and an infected vaginal cuff 10 days after hysterectomy (1 patient each).

The pack was usually left in for about 36 hours with a weight on the tail for the first 24 hours. A 1000 cc. bottle of intravenous fluid was used as a weight. The pressure exerted on the bladder by the pack was about 40 mm. Hg. as measured through a foley catheter in one patient. This pressure was increased to 50 mm. Hg. when 2 bottles of fluid were used as a weight.

Complications

A problem with removal occurred the first time the pack was used. Care was not taken to prevent tangling of the gauze in making the pack for abdominal insertion. This pack was difficult to remove vaginally and general anesthesia was required. Now, tangling is avoided in making the pack for abdominal insertion. Obviously, there is no problem with vaginal application. The gauze simply comes out opposite to the way it went in (Figure 3).

Bladder pressure was sufficient to obstruct urine flow in one patient during the time the weight was used. More than 400 cc. of urine were passed in the first half-hour after the weight was removed. None of the patients had serious infections. Moreover, effective control of bleeding seemed more important than danger of infection from using the pack.

Conclusions

The umbrella pack seems to be particularly effective in quickly controlling hemorrhage from several sources: large raw surfaces, venous plexuses, and inaccessible areas. Suturing is difficult or ineffective under these conditions. Pressure from packing is the only solution. However, packing the pelvis with loose gauze in the usual manner has several disadvantages: positive pressure on bleeding points is eliminated as soon as the abdomen is closed since intra-abdominal pressure is zero, and loose gauze packing will not control bleeding from any artery. The umbrella pack solves both these problems.

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AMA REAFFIRMS STAND ON CHIROPRACTIC

At its meeting in San Francisco, June, 1968, the AMA House of Delegates adopted a resolution which urged constituent state societies and component county associations to take official cognizance of the AMA Statement of Policy on Chiropractic (November, 1966), and to "alert the general public to the health hazard posed by the cult of chiropractic."

Accordingly, the full statement of policy of the American Medical Association on this subject is reproduced herewith for the information of the membership:

Statement of Policy

It is the position of the medical profession that chiropractic is an unscientific cult whose practitioners lack the necessary training and background to diagnose and treat human disease. Chiropractic constitutes a hazard to rational health care in the United States because of the substandard and unscientific education of its practitioners and their rigid adherence to an irrational, unscientific approach to disease causation.

In 1965, a United States District Court, in upholding a state's constitutional right to refuse to license chiropractors, said that "since chiropractic claims to be a complete and independent healing art capable of curing almost all kinds of disease, the state Legislature may have felt that the requirement of a foundation in materia medica and surgery . . . would be a protection to the public." Without dissent, the United States Supreme Court affirmed the decision.

The wisdom of these decisions by the nation's highest courts justifies the medical profession's educational program of alerting the nation to the public health threat posed by the cult of chiropractic.

Patients should entrust their health care only to those who have a broad scientific knowledge of disease and ailments of all kinds, and who are capable of diagnosing and treating them with all the resources of modern medicine. The delay of proper medical care caused by chiropractors and their opposition to the many scientific advances in modern medicine, such as life saving vaccines, often ends with tragic results.

Dietary Management in Chronic Renal Disease

Marilyn Lawler, M.S.

In recent years widespread interest has been shown in the management of chronic renal disease. While attention has focused on dialysis and the consequent improvement of clinical symptoms and biochemical abnormalities, this technique represents only a partial approach to the management of selected patients. It does not substitute for a well-planned dietary regimen (which is an integral part of treatment) or for strict control of fluid and electrolyte balance. Moreover, not all patients with chronic renal disease are suitable candidates for dialysis. For many with severe renal insufficiency, dietary modification, together with careful medical management, offers the most reasonable hope for relief of symptoms.

Reduction of the intake of protein is not necessary (and may be contraindicated) in patients with only mild elevation of blood urea nitrogen (BUN) or in the nephrotic syndrome. On the other hand in severe chronic renal insufficiency, when symptoms of uremia are present, the BUN is more than 80 mg per 100 ml, and the creatinine clearance is from 3 to 10 ml per minute, there is often symptomatic improvement when dietary protein is restricted.

As renal insufficiency progresses, retention of nitrogenous end-products increases. The role of protein in increasing urea production has been well-established; likewise, reduction in nitrogenous wastes has been associated with a low protein intake. The optimal level of protein intake is not entirely clear. Levels of 0.26 to 0.5 gm. per kilogram of body weight per day have been recommended as the minimum amount required to prevent depletion of body proteins while limiting production of urea[1 2]. Thus, for a 70 kilogram man, from 18 to 35 grams of protein per day are needed.

On such a limited protein intake, consideration must be given to the type of protein offered. For maximal efficiency in meeting the body requirement for protein, the diet should provide protein of high biological value; that is, protein containing all the essential amino acids in sufficient proportions to meet body needs. It has been demonstrated that as little as 2 gm. of nitrogen daily from essential amino acids or egg protein is sufficient to maintain nitrogen equilibrium while lowering markedly elevated blood urea nitrogen to near normal levels in uremic patients[3 4]. Such a diet provides a minimal intake of non-essential amino amino acids, thereby enabling the patient to utilize his accumulated urea nitrogen for protein synthesis. Other investigators[5] have recently shown that small amounts of protein of lower biological value (i.e., cereals and vegetables) can be added to a low protein diet without appreciably increasing protein catabolism. It seems reasonable to expect that these additional foods would contribute much to the acceptability of the diet because of the greater variety in selection they allow the patient.

Several groups of investigators[3-7] have shown that utilization of dietary protein is enhanced when liberal amounts of carbohydrate and fat are ingested simultaneously with the protein. Intake of these substances must be great enough to meet caloric needs and to prevent degradation of endogenous proteins. While emphasis on adequate caloric intake is an essential part of the dietary management, frequently anorexia, nausea and vomiting are limiting factors to optimal nutrition. Vitamin and mineral supplementation may be needed to prevent deficiencies of the B vitamins, ascorbic acid, calcium, and iron. Intake of these substances may fail to meet the recommended dietary allowances because of the multiple dietary restrictions imposed, and as a consequence of the anorexia and nausea which commonly occur.

The hyperkalemia often associated with oliguria in chronic renal disease may require moderation of potassium intake. This is only partially accomplished by limiting the protein intake, and significant contributions made by liberal use of fruits and vegetables must not be overlooked.

Presence of edema, hypertension, and threat of congestive heart failure may further modify the

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diet by imposing a sodium restriction over and above that achieved by use of a low protein diet. By using foods prepared without the addition of sodium compounds, the daily sodium intake can be reduced to 250 mg. if necessary.

Rigid control of fluid intake is often necessary to prevent edema formation. The total daily allowance, as determined by urine volume, extrarenal losses, and considering the amount formed from the oxidation of food (about 400 ml), (2) may amount to less than a liter per day.

The challenge to the dietitian is successfully met only when she has planned a diet which is acceptable to the patient while meeting the above requirements. In planning the diet, considerable time and effort can be saved by devising a basic plan which can be adapted to the needs of various individuals. This can be done by grouping foods according to protein and potassium contents and adjusting amounts allowed from each group as indicated by the individual diet order. Average protein and potassium contents for several such food groups, as compiled from food composition tables (8), are listed in Table I. Foods containing large amounts of potassium and/or sodium can be eliminated from the groups (Table II) in order that the plan might be used for a greater number of patients; however, the greatest possible variety of foods, within the limits of the diet prescription, must be allowed in order to assure the continued co-operation of the patient.

TABLE I

AVERAGE PROTEIN AND CONTENTS OF SEVERAL FOOD GROUPS

Food Group	*Weight (gm.)*	*Household Measure*	*Protein (gm.)*	*Potassium (mg.)*
MILK	240	1 cup	8.0	335
EGG	50	1 egg	7.0	65
MEAT, FISH POULTRY	30	1 oz.	7.0	100
CHEESE	30	1 oz.	7.0	25
VEGETABLES				
I	*	*	1.0	140
II	*	*	2.0	170
III	*	*	3.0	200
FRUITS				
I	*	*	0.5	100
II	*	*	1.0	150
BREADS AND CEREALS	*	*	2.0	27
POTATO	100	½ c.	2.0	360
FATS				
Butter	5	1 tsp.	—	1
Oils	5	1 tsp.	—	—
Cream	30	1 oz.	1.0	34
SWEETS	5	1 tsp.	—	5

* Amount varies with foods in this group.

TABLE II

FOOD GROUPS ACCORDING TO PROTEIN AND POTASSIUM CONTENT

MILK CHOICES

(1 cup equals 8 gm. protein, 335 mg. potassium)

Allowed

Buttermilk, unsalted
Evaporated milk, reconstituted
Low sodium milk
Nonfat buttermilk, unsalted
Nonfat dry milk, reconstituted
Whole milk
Skim milk

Avoid

Any other milk
Commercial foods made of milk:
  ice cream, sherbet, milkshakes, chocolate milk, malted milk, milk mixes, condensed milk, etc.

MEAT CHOICES OR SUBSTITUTES

(1 ounce, cooked, (30 grams) equals 7 gm. protein, 100 mg. potassium.)

Allowed

Beef, chicken, duck, lamb, liver, pork, turkey, veal, tongue (unsalted)

Avoid

Kidneys, brains
Canned, salted, or smoked meats as:
  bacon, bologna, chipped beef, corned beef, frankfurters, ham, Kosher meats, luncheon meats, salt pork, sausage, smoked tongue
Other meats

Allowed

Cod, flatfish (flounder and sole), Kingfish (whiting), haddock, perch, salmon, tuna (unsalted)
*Clams, *crab, *lobster, *oysters, *scallops, *shrimp

Avoid

Frozen fish fillets
Canned, salted, or smoked fish:
  Anchovies, caviar, cod (dried and salted), herring, halibut, sardines

Allowed

Egg (1 egg equals 7 gm. protein, 65 mg. potassium.)
*Cheese (1 ounce equals 7 gm. protein, 25 mg. potassium.)
  Cheddar (domestic)
  Cottage, American, Swiss

Avoid

Other cheeses
Peanut butter

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* Omit on Sodium Restricted diets; use low sodium variety.

VEGETABLE CHOICES

Group I (1 gm. protein, 140 mg. potassium per serving.)

Allowed

½ cup serving (100 grams)
*Beets, fresh or canned
Cabbage, raw or cooked
*Carrots, fresh, canned or raw
*Celery, raw
Cucumber, raw pared
Eggplant, cooked
Endive, raw
Lettuce, Iceberg or Romaine
Onion, cooked
Rutabagas, cooked
Squash, summer
Tomato, cooked
*Turnips, cooked
¼ cup serving (50 grams)
Onion, raw
Tomato, raw

Group II (2 gm. protein, 170 mg. potassium per serving.)

Allowed

½ cup serving (100 grams)
*Dandelion greens, cooked
Green beans, fresh, canned, frozen
Wax beans, fresh, canned, frozen
Cauliflower, fresh or frozen
Corn, cream style, canned
Mustard greens, cooked, or frozen
Okra, fresh, cooked, or frozen

Avoid

¼ cup serving (50 grams)
*Succotash, frozen
Brussels Sprouts, fresh or frozen
*Peas, canned or frozen
Squash, winter, mashed

Group III (3 gm. protein, 200 mg. potassium per serving.)

Allowed

½ cup serving (100 grams)
Asparagus, fresh, canned or frozen
Broccoli, fresh or frozen
*Collards, cooked
Corn, W.K., fresh, canned, or frozen
*Kale, cooked (leaves and stems)
*Mixed vegetables, frozen
*Spinach, fresh, canned, or frozen
¼ cup serving (50 grams)
Lima beans, canned

AVOID THE FOLLOWING VEGETABLES

Artichokes; Beans, dried; Beans, Lima (frozen); Chard, Swiss; Parsnips; Peas, split; Sauerkraut; Spinach, fresh and frozen; Squash, winter (baked)

FRUIT CHOICES

Group I (Less than 0.5 gm. protein, 100 mg. potassium per serving)

Apple raw	1 small
Applesauce	½ cup
Fruit Cocktail	½ cup
Grapes, European	12
Peaches, canned	½ cup
Pears, canned or fresh	½ cup
Pineapple, canned	½ cup
Plums, canned	½ cup
Apple Juice	½ cup
Apricot Nectar	½ cup
Cranberry Juice Cocktail	½ cup
Grape Juice	½ cup
Orange-Apricot Juice	½ cup
Peach Nectar	½ cup
Pear Nectar	½ cup
Pineapple Juice	½ cup
Pineapple-Grapefruit Juice	½ cup
Pineapple-Orange Juice	½ cup

Group II (1 gm. protein, 150 mg. potassium per serving)

Apricots, canned	½ cup
Blueberries, fresh or frozen	½ cup
Boysenberries, canned, frozen	½ cup
Cherries, canned	½ cup
Figs, canned	½ cup
Grapefruit, fresh, canned	½ cup
Orange	1
Strawberries, fresh or frozen sliced	½ cup
Tangerine	1
Watermelon	½ cup
Grapefruit Juice, unsweetened	½ cup
Grapefruit-Orange Juice	½ cup
Orange Juice, frozen	½ cup
*Tomato Juice, canned	½ cup

AVOID THE FOLLOWING FRUITS

All dried and frozen fruits with sodium sulfite added; Apricots, fresh; Avocado; Bananas; Pumpkin; Maraschino Cherries; Crystallized and glazed fruits; Nectarines; Rhubarb; Peaches, fresh; Prunes; Raisins

BREADS AND SUBSTITUTES

(2 gm. protein, 27 mg. potassium per serving)

Bread	1 slice
Cereals, dry:	1 cup
Cornflakes	
Puffed Rice	
Puffed Wheat	
Shredded Wheat	
Cereals, cooked:	½ cup
Cornmeal	
Farina	
Oatmeal	
Rice	
Rolled Wheat	
Crackers, soda	3 squares

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* Omit on Sodium Restricted Diets; Use Low Sodium Pack Canned Vegetables.

Flour	2 Tablespoons
Grits	1 cup
Macaroni, Noodles or Spaghetti	¼ cup
Rice	½ cup
Potato	½ cup or 1 medium

(NOTE: Average potassium for potato is 360 mg.)

AVOID THE FOLLOWING BREADS AND SUBSTITUTES

Yeast breads or rolls or Melba toast made with salt or from commercial mixes.

Quick breads made with baking powder, baking soda, or salt, or made from commercial mixes.

Quick-cooking and enriched cereals, which contain a sodium compound.

Commercial baked products.

Dry cereals except for those listed as allowed.

Self-rising cornmeal.

Graham crackers or any other crackers except low-sodium dietetic.

Self-rising flour.

Salted popcorn.

Potato chips.

Pretzels.

Waffles containing salt, baking powder, baking soda, or egg white.

FATS

(Negligible protein and potassium)

Allowed

*Butter
Cream, light or heavy
Fat or cooking oil (unsalted)
*Margarine
*Salad dressings: French or Mayonnaise

Avoid

Avocado
Bacon, bacon fat
Olives
Nuts
Salt Pork

(NOTE: 1 ounce cream contains 34 mg. potassium.)

MISCELLANEOUS

Allowed

Cornstarch
Gingerale
Hard Candies
Honey
Jam or jelly
Jellybeans
Rice starch
Spices
Sugars
Syrup
Tapioca, granulated
Vinegar
Wheat starch

Avoid

Antacids, laxatives
Canned, dried, frozen soups
Chocolate
Cocoa, instant cocoa mixes
Coconut
Prepared beverage mixes, including fruit flavored powders
Fountain beverages
Other commercial candies
Commercial gelatin desserts
Regular baking powder and soda
Rennet tablets
Molasses
Pudding mixes
Most other carbonated beverages

SEASONINGS

Allowed

Allspice
Almond extract
Anise seed
Basil
Bay leaf
Caraway seed
Cardamon
Catsup (dietetic)
Chili powder
Chives
Cinnamon
Cloves
Cumin
Curry
Calcium cyclamate
Dill
Juniper
Lemon juice or extract
Mace
Maple extract
Marjoram
Mint
Mustard (dry)
Nutmeg
Orange extract
Oregano
Paprika
Pepper
Peppermint extract
Pimiento
Poppy seed
Purslane
Rosemary
Saffron
Sage
Savory
Sesame seeds
Sorrel
Tarragon
Thyme
Tumeric
Vanilla extract
Walnut extract

Avoid

Bouillon, Broth
Consomme
Catsup, regular
Celery leaves (dried or fresh)
Celery Salt
Chili Sauce
Cyclamate, sodium
Garlic salt
Horseradish, prepared
Meat extracts, sauces, and tenderizers
Monosodium glutamate
Mustard, prepared
Onion salt
Pickles
Relishes
Salt and salt substitutes
Soy sauce
Worcestershire sauce

In this plan, the basic low protein diet (20 gm.) includes 1 egg and 6½ ounces of milk daily; other protein containing foods are added in amounts consistent with the diet order. Meats are omitted until the diet order approaches 40 gm. protein. Low protein breads (9) and desserts are useful adjuncts for providing calories with minimal amounts of protein. In areas where low protein breads are not available, use of regular bread is limited to one slice daily at the 20 gm. protein level. Liberal use of pure carbohydrates and fats is needed to insure adequate caloric intake. Requirements for the essential amino acids are met with the exception of methionine. Phenylalanine and tryptophan are marginal, however. The diet does not meet the Recommended Dietary Allowances for the B-complex vitamins, iron, or calcium; therefore, oral supplements may be needed.

A sample menu (Table III) included, if planned according to commonly used exchange list values for protein, fat, and carbohydrate, provides approximately 20 gm. protein, 60 gm. fat, 300 gm. carbohydrate, and 1800 calories. When the same menu is calculated from values in food composition tables (8, 10), it is found to provide 23 gm. protein, 56 gm. fat, 300 gm. carbohydrate, and 1800 calories, 825 mg. sodium, and 1225 mg. potassium. Water content of solid foods and liquids is approximately 1200 cc. In this menu, all cooked foods are unsalted and low sodium canned vegetables are used; sodium content can be reduced to approximately 230 mg. by using unsalted bread, butter, and mayonnaise. The menu can be increased to 40 gm. protein with the addition of 2 ounces of meat and use of regular bread in place of low protein bread.

TABLE III

SAMPLE MENU

20 GRAM PROTEIN DIET

Food	*Amount*	*Wt. (gm)*
Breakfast		
Grapefruit Sections	⅓ c.	70
Cornflakes, (Low Sodium)	¾ c.	20
Low Protein Bread	1 slice	20
Butter	1 tsp.	5
Jelly	2 tsp.	10
Milk	½ c. - 2T	90
Tea	3½ oz.	100
Sugar	2 tsp.	10
Lunch		
Poached Egg	1	50
Rice	½ c.	100
Butter	1 tsp.	5
Green Beans	½ c.	100
Butter	1 tsp.	5
Lettuce	5 sm. lv.	50
Oil and Vinegar Dressing	1 tsp. ea.	10
Low Protein Bread	1 slice	20
Butter	1 tsp.	5
Jelly	2 tsp.	10
Low Protein Tapioca Pudding	1 serv.	85
Gingerale	3½ oz.	100
Mid Afternoon		
Hard Candies	5 pc.	25
Dinner		
Fruit Plate:		
Peaches, Canned	2 halves	100
Pears, Canned	2 halves	100
Strawberries, Frozen	5	50
Lettuce	2 lg. lvs.	25
Mayonnaise	2 tsp.	10
Low Protein Bread	1 slice	20
Butter	1 tsp.	5
Jelly	2 tsp.	10
Milk	½ c. - 1T	105
Low Protein Cookie	2	20
Bedtime Snack		
Cranberry Juice Cocktail	¾ c.	180

In spite of careful medical management and good dietary control, the accumulation of nitrogenous compounds, sodium, potassium, and water, may occur as the disease progresses. For some patients, chronic intermittent dialysis (peritoneal or hemodialysis) is an effective means of removing excesses when conservative treatment fails; between dialyses, however, adherence to a well planned dietary regimen is essential if increments are to be kept at a minimum. The need for close co-ordination of dietary and medical management is evident.

The success of any diet depends, to a great extent, upon the patient's understanding of, and acceptance of, the diet planned for him. Frequent counselling in regard to diet, and individualization of any basic plan used are necessary if dietary indiscretion by the patient is to be kept at a minimum. The level of adherence to the diet reveals the effectiveness of the instructions. In chronic renal disease, amelioration of gastrointestinal symptoms and return of appetite are further indications of compliance with the dietary regimen. Dietary management in this disease can be a challenge to the ingenuity of the dietitian and patient alike.

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Announcing The

MARTHA LOUISE CLIFFORD, M.D., MEMORIAL FUND

Dear Friend:

We presume that you, like the many other friends and associates of Dr. Martha Louise Clifford are feeling the loss caused by her untimely death. She was a much beloved and admired professional worker and outstanding human being. Dr. Clifford had served in the Connecticut State Department of Health for years, and was Director of the Community Health Division during her later years. Many persons have expressed their wish to contribute to a living memorial.

Recently a committee composed of persons from various fields of professional interest, and drawn from local, state, and national levels, proposed the establishment of a Martha Louise Clifford, M.D., Memorial Fund. This fund would assist women, who are studying at the University of Connecticut, towards a career related to Maternal and Child Health, Pediatrics, or Public Health; and who may need special financial assistance to maintain themselves in their college program. The University educates physicians, nurses, nutritionists, health educators, social workers, rehabilitation workers, and other professional health workers. Through this memorial fund, Dr. Clifford's interest would continue.

The University of Connecticut, through its counselling services in appropriate departments and schools will make the awards. The University of Connecticut Foundation has arranged to assist in the development of the Fund, in order to encourage women in the pursuit of careers in health services.

We hope you will share in this effort to make a successful commemoration of Dr. Clifford. Checks may be made payable to the Martha L. Clifford, M.D., Memorial Fund, and sent to the University of Connecticut Foundation, University of Connecticut, Storrs, Connecticut, 06268.

Sincerely,

Ira V. Hiscock, Sc.D.
Conn. Public Health Council and
Emeritus Professor, Yale University

Toward the Understanding of Ingrown Toenail

Gerald O. Strauch, M.D.

During a period in which medicine is making such gigantic strides, in which artificial and transplanted vital organs are no longer sheer fantasy, the physician may be tempted to dismiss many smaller problems with little thought. Especially is this easy dismissal of "minor" problems apt to infuse these who can afford such an attitude the least, namely, physicians in training. The late Dr. Frederick A. Coller asserted that there is no minor surgery, though he conceded the existence of many minor surgeons.

One such minor problem is that of the ingrown toenail. Unlike many surgical diseases which require minimum operative effort on the part of the physician managing the case, this malady possesses several characteristics which allow for the perpetuation of error in management. First, almost any mode of therapy which even temporarily destroys the relationship between the nail and the soft tissue which the nail violates will temporarily ameliorate symptoms. Second, unsatisfactory results may be tolerated by the patient as long as pain is relieved, since appearance and vital functions are not significantly compromised. Finally, there is a tendency for the ingrown toenail to rectify itself under certain circumstances.

The Pathogenesis Of Ingrown Toenail

Many discussions of ingrown toenail have it that tight, illfitting shoes or stockings are basic in etiology[1]. Abnormalities related to weight-bearing are emphasized by Vandenbos and Bowers[2]. Abnormal nail curvature is implicated by Larmon[3].

It seems apparent to this author that habitual faulty trimming of the nail is the basic mechanism in the pathogenesis of the ingrown toenail, and that this can be well documented by careful history taking, the findings at operation, and the results of treatment in these cases. Certainly one sees rare cases in which deformed toes, the result of trauma, congenital deformity, or disease, are basic etiologically. Again, toenails deformed by trauma, onychomycosis, or other disease processes rarely may be central in the initiation of the process. In the usual case, however, the fault lies in the patient's poor habits in toenail hygiene.

The evolution in most cases can be described with little difficulty. Over a period of months or years, the patient trims the large toenails with a curvilinear cut. No problem develops as long as the nail is trimmed completely to its lateral margin, although the absence of the nail's extension over its entire normal coverage of the dorsum of the distal phalanx allows for piling up of soft tissue in the area adjacent to the nail. *The difficulty arises when, by accident or carelessness or technical difficulty, a fragment of the nail remains untrimmed at the lateral margin and covered by soft tissue.* Now, as the nail continues to grow, this fragment is driven progressively deeper into the soft tissue, at the same time becoming more inaccessible for removal. This encroachment on the soft tissue is painful, and the pain is the first symptom suffered by the patient. (The pain, of course, will be aggravated by any secondary force, such as tight shoes or stockings, which increases pressure of the ragged nail on the soft tissue, but these forces only amplify the symptoms and are not the source of the disorder.) The nail is now functioning as a foreign body. With continued nail growth, penetration of the skin may occur, and granulation tissue may begin to form and pile up. This process will then tend to set up a vicious cycle is which the nail stimulates more granulation and the granulation tissue provides more of a barrier to the spontaneous cure which might otherwise result. Frequent secondary bacterial invasion, which produces typical active chronic paronychia, completes the familiar full-blown picture.

If, at any point in the evolution, the nail breaks through the soft-tissue barrier which has obstructed its way, a spontaneous cure results.

The crux of the problem, then, is the existence of the abnormal interface between the advancing corner of the growing nail and the periungual soft tissue.

DR. GERALD O. STRAUCH, Attending Surgeon, Stamford Hospital and Attending Surgeon, St. Joseph's Hospital, Stamford, Conn.

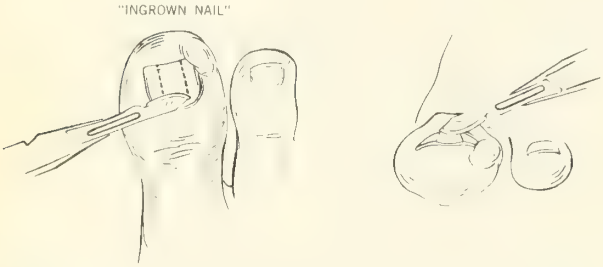
The Treatment Of Ingrown Toenail

With the above in mind, it seems simple to outline a rational approach to the treatment of this annoying affliction.

The vast majority of cases are completely preventable, simply by educating the patient regarding proper trimming of the great toenails. A straight cut across the distal nail at a point where full visualization of the lateral nail margins is always afforded will effectively prevent ingrown toenail.

When the uncomplicated ingrown toenail is encountered in a patient who has only incipient discomfort due to pressure of the nail on the soft tissue, without gross granulation tissue and paronychia, the aim should be to encourage spontaneous resolution. The patient should be told that this will encompass several weeks and that he can expect some discomfort whenever pressure is exerted over the affected corner of the nail. Here the maneuver of shaving the center portion of the nail may offer some relief from discomfort to the patient while the nail undergoes its necessary growth (Figure 1.). Packing of the soft tissue away from the nail or of cotton under the nail are not only painful but usually ineffective, and may precipitate paronychia formation. When the nail has finally emerged from its abnormal situation, correct trimming of the nail is all that remains necessary.

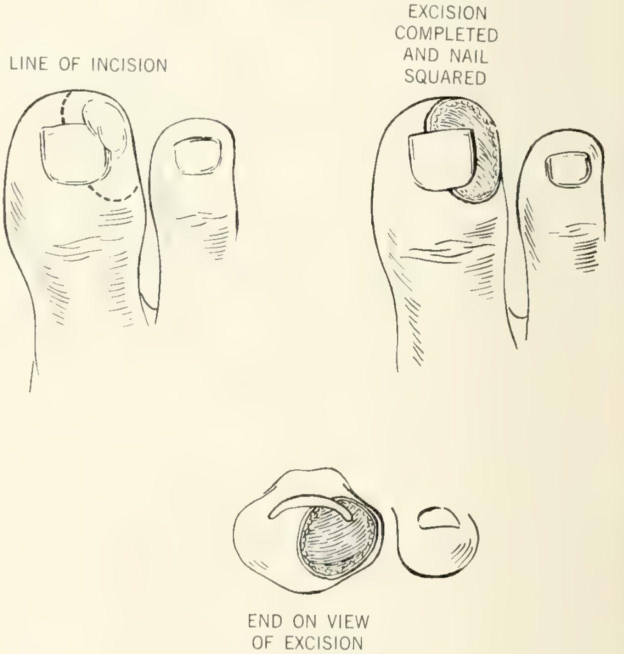
Figure 1



Method of shaving of central portion of nail to decrease pressure on periungual tissues by nail margin.

Treatment of the patient who presents with the complete picture of ingrown toenail and resultant paronychia must be aggressive. It must also be properly conceived to accomplish its purpose in a definitive and permanent manner. Since the site of impingement of nail on soft tissue must be eliminated to effect a cure, either nail or soft tissue must be removed. Removal of the nail locally will not be curative since regrowth will be accompanied by return of symptoms. Although advocated in most textbooks, excision of a complete longitudinal segment of the nail, with or without destruction of the matrix of the segment, seems illogical, since the nail is not basically abnormal; further, trauma to the nail matrix is followed by regrowth of a deformed abnormal nail more frequently than not. Removal of the bulbous soft tissue surrounding the affected nail, then, is the most rational and effective means of eradication of the disease. The excision of the soft tissue must be generous so that by the time re epithelialization is complete, adequate nail growth has occurred to prevent recurrence of the condition. In addition, the excision should include all excess periungal soft tissue which might be involved in the future under similar circumstances. These requisites can be met by excision, from around the involved side of the nail, of a wide margin of skin and subcutaneous pulp of the distal phalanx of the toe, from the base of the nail (eponychium) to the midpoint of the free margin of the nail (Figure 2.). The resultant defect will usually be about 1.5 cm. in width and will extend to bone in depth. Digital block of the hallux is a convenient form of anesthesia for the procedure, although in patients, such as diabetics, where peripheral vascular problems might be anticipated, general or regional anesthesia may be preferable.

Figure 2



Extent of excision of periungual tissue for cure of ingrown toenail.

Any element of active cellulitis can usually be controlled by saline soaks for several days prior to operation, and neither systemic nor local antibiotics are usually necessary or desirable. Bleeding is profuse enough to require a bulky dressing initially. Within forty-eight hours following operation, intermittent saline soaks are initiated. Though discomfort is present to some degree for only five to ten days, healing requires several weeks for completion. Continued care includes only proper toenail trimming.

The author has never experienced failure in the management of these cases by this simple systematic approach, and it is difficult to conceive of failure, except under very unusual circumstances, in the ordinary case. This is in agreement with the experience of Vandenbos and Bowers with a similar type of operation. It is amazing, however, how many recurrent and so-called "resistant" cases one encounters which seem to reflect poorly conceived therapeutic efforts rather than difficult therapeutic problems.

Conclusion

It appears that vexing experience with ingrown toenail may be the result of faulty treatment, advocated in textbooks for years, based on erroneous concepts of the pathogenesis of the condition. With the many difficult problems the physician faces daily, it seems a pity that treatment of the ingrown toenail should present any difficulty whatsoever. Treatment directed at spontaneous resolution of the condition in early cases or at elimination of the soft tissue barrier to nail growth in late cases seems to offer a welcome solution.

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> "Were it in my power to do so I would . . . leave you with a gift. Not wisdom which I have not and no man can give, but the next best thing: the love of wisdom for which philosophy is but another word. For to love wisdom is also to love science and prudence: it is to seek peace in the inner accord of each mind with itself and in the mutual accord of all minds."
>
> —*Etienne Gilson*

The Hartford Hospital Interdepartmental Conference

Fever of Obscure Etiology

Moderator: Ronald P. Kaufman, M.D.

Dr. Ronald Kaufman (Moderator)

Today we are presenting fever of obscure origin, to provoke stimulating questions, and perhaps supply some answers. We have on our panel, Doctors Reinfrank, Pyrtek, Burchell, and Bartlett.

Dr. Gary Nobert

This was the first pregnancy in a 15-year-old, single girl, admitted at term in active labor. The only significant past history was reputed rheumatic fever at age six, without documentation or history of heart murmur. The vertex was not completely engaged. By x-ray pelvimetry the pelvis was small, ovoid, but the estimated intraspinous diameter was judged adequate for a trial of labor. She delivered after moderate difficulty by low forceps a normal 8 lb., 12 oz., boy. Because of considerable intrapartum hemorrhage, the uterus was explored twice, but no laceration was found. Bleeding was controlled with intravenous oxytocin and uterine massage. The vaginal mucosa was found to be extensively lacerated and was repaired. On the evening of the first postpartum day, the patient's temperature rose to 101°F. No cause was found. Thereafter, the temperature daily reached 103°F. The working diagnosis was urinary tract infection, and on the third postpartum day ampicillin was started.

Dr. Kaufman

I would like to poll the panel members as to their differential diagnosis of postpartum fever.

Dr. Ralph F. Reinfrank

There are several likely possibilities: (1) retained secundines, (2) urinary tract infection, perhaps the result of delivery or urinary tract instrumentation, (3) thrombophlebitis. Pregnancy and the manipulation of delivery makes any female a candidate for thrombophlebitis in the pelvis or legs.

Dr. Kaufman

Dr. Pyrtek, would this fit with your thinking or is there some particular surgical consideration that would lead you one way or the other?

Dr. Ludwig J. Pyrtek

Other possibilities, of course, include appendicitis or gallbladder disease, but these would be unlikely in the absence of other symptoms.

Dr. Clay Burchell

Such high fever is unusual so early postpartum. I would think first of mastitis or urinary tract infection. If the patient had bacteriuria before delivery, she might now be having a urinary tract infection. Pelvic infection rarely causes such a high fever this soon after delivery. Back in the days before antibiotics, classical puerperal sepsis usually occurred on the eighth or ninth day, followed by peritonitis and ending in death. Mastitis can cause such a high postpartum fever, but it is rare prior to about the seventh day. I have seen another group of patients with postpartum spiking fever who have positive blood cultures but recover without antibiotics. Perhaps some patients get a bacteremia from delivery. Concerning this case, I would think first of urinary tract infection.

Dr. Kaufman

The staff apparently also felt this was a urinary tract infection but could not prove it. Subsequent urine cultures grew 1+ E. coli. Dr. Burchell, would you have started ampicillin empirically on the clinical impression that this was urinary tract infection?

Dr. Burchell

Yes, after the culture was started.

Dr. Kaufman

Dr. Bartlett, what does a 1+ E. coli mean in the urine? Are colony counts more meaningful?

Dr. Raymond Bartlett

The true significance of both the colony count and the qualitative plating technique depends on

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Discussants:

Gary Nobert, M.D., (Resident Physician, Ob-Gyn)
Ralph F. Reinfrank, M.D., (Director, Dept. of Internal Medicine)
Ludwig J. Pyrtek, M.D. (Senior Staff, Dept. of Surgery)
Clay Burchell, M.D., (Director, Dept. of Ob-Gyn.)
Raymond Bartlett, M.D., (Chief Section on Microbiology, Dept. of Pathology)
Jack L. Wescott, M.D., (Dept. of Radiology)

DR. RONALD P. KAUFMAN, Director, Department of Medical Education, Assistant Director, Department of Medicine, Hartford Hospital, Hartford, Conn.

proper handling of the specimen. Urine poorly collected or delayed more than five hours on the way to the laboratory is not going to give valuable information whether it is a colony count or just a stick plate. There is a close correlation between 1+ or 2+ bacterial growth and fewer than 100,000 colonies. A colony count is now done by a calibrated loop innoculated onto a melted plate of agar and streaked around the plate. The traditional plating technique streaks the specimen on a plate, using a loop which is not closely calibrated. The two methods are really quite similar.

Dr. Kaufman

Apparently most of us agree ampicillin would be started after appropriate studies had been initiated. Then, what happened?

Dr. Nobert

The temperature spike continued daily. Pelvic exam on the fifth postpartum day revealed a separation of the lower perineal portion of the episiotomy but there was no abscess or endometritis. The hematocrit was 29%, and she received two units of packed red cells, bringing the hematocrit to 37%. Clinically, she appeared surprisingly well except for chills at the time of the temperature spikes. The white count was not elevated, but there was a slight shift to the left. All the cultures were unrevealing. The serum LDH and alkaline phosphatase were moderately elevated. The diagnosis of subdiaphragmatic abscess was also considered, but the diaphragms were radiographically normal. There was no evidence of subacute bacterial endocarditis. The IVP was normal. Despite the essentially normal pelvic examination, pelvic vein thrombophlebitis was considered possible. Chloromycetin was added on the sixth postpartum day and intravenous penicillin was substituted for ampicillin on the eighth day.

Dr. Kaufman

Other questions now come to mind. Here was a past history of rheumatic heart disease, and her hematocrit was now falling. Dr. Reinfrank, would you consider subacute or acute bacterial endocarditis?

Dr. Reinfrank

I always consider subacute or acute bacterial endocarditis in a febrile patient who has had rheumatic fever, but there was nothing in this history or physical examination that indicated she had ever had heart disease. Many illnesses have been referred to as rheumatic fever. However, there was no definite evidence of heart disease, no positive blood cultures, and there are many other reasons in this patient for a fever. In this case, the probability is remote.

Dr. Kaufman

Dr. Bartlett, how many blood cultures are needed statistically to get into the ninetieth percentile, how should they be cultured, and how collected?

Dr. Bartlett

The consensus is that you will get upwards of ninety per cent yield after the third blood culture in gram-negative bacteremia, and similar statistics have been reported in subacute bacterial endocarditis, but there is still considerable debate about it.

Dr. Burchell

Can you be a little more specific about three blood cultures? Can you take three bottles at one sitting, or at three different times, or different arms, or what?

Dr. Bartlett

Some people feel it is purely the volume of blood, and not the number of aliquots or the frequency with which they are taken. At Hartford Hospital, we use a 100 ml flask to allow us to get a ten ml innoculum of blood. By diluting at least 1 to 10 in broth medium, antibodies and antibiotics are diluted. There is still much controversy about the value of adding neutralizers such as magnesium, neutralized tetracycline, penicillinase, or cephalosporinase. We consider it adequate to dilute a large volume of blood in a large volume of broth and therefore use 10 ml of blood in 100 ml broth. Concerning aerobic and anaerobic cultures, you can't culture both together. Bacteroides was never cultured in this hospital until five years ago; we just didn't isolate it. Now we find bacteroides frequently, and it's an important anaerobic organism. It is cultured only by strict anaerobic methods. If a series of blood cultures is obtained from one patient, we try incubating some aerobically and some anaerobically. We recommend you collect two bottles simultaneously: one labeled aerobic, the other anaerobic. As for collection, alcohol is a fine disinfectant. Preparation of the skin with alcohol is ideal for the collection of blood cultures.

Dr. Kaufman

Dr. Reinfrank, after three days of ampicillin, chloramphenicol was added, and 48 hours later ampicillin was stopped. What do you think of this approach?

Dr. Reinfrank

In general, if one does not know the source of fever, it is not a good approach. By the eighth or ninth day, one is faced with the question: is it the antibiotic that is now causing the fever rather than the original illness? Secondly, at least in a number of patients, this approach results in super-infections, bringing even more difficult problems. I believe one should hold out as long as possible for an etiologic diagnosis unless the situation is desperate. One should not change antibiotics capriciously.

Dr. Kaufman

How high does drug fever go?

Dr. Reinfrank

Drug fever can mimic any fever, low grade, spiking, or hectic.

Dr. Kaufman

Dr. Pyrtek, from a surgical point of view, would you have added these drugs in this sequence?

Dr. Pyrtek

Apparently, urinary tract infection was the most likely probability. Having chosen ampicillin, which is currently popular for this, a little longer trial would have been indicated. If no response had been obtained, I might then have discontinued the antibiotics and searched again for some other cause of the illness. By and large, a urinary tract infection is usually clarified in two or three days. When the result is inadequate, you should suspect something else is the cause of the illness.

Dr. Kaufman

So you agree it was alright to start ampicillin on clinical grounds and statistical chance, to be continued for perhaps five days and if the response is inadequate, perhaps stop and re-evaluate the situation.

Dr. Bartlett

Would anybody feel justified in starting a "sulfa" drug, rather than going right to ampicillin?

Dr. Reinfrank

I don't see any excuse for the existence of "sulfa" drugs or their use in the hospital setting. In this case, with this type of fever, pyelonephritis is postulated and a "sulfa" drug is just not appropriate. I think "sulfa" is most successful if the doctor doesn't see the patient three weeks later. The patient seems to get well, but another physician will pick up the second, the third, the fourth, and the fifth urinary tract infections.

Dr. Kaufman

Dr. Nobert, what developed next?

Dr. Nobert

On the eleventh postpartum day, all drugs were discontinued to exclude drug fever. The next day the temperature went over 103°F. Heparin was started to treat a possible septic pelvic thrombophlebitis. There was no evidence of pulmonary emboli. The fever persisted. Heparin was discontinued and I.V. cephalothin started on the sixteenth day. On the seventeenth day the patient had a dilatation and curettage to exclude infected retained secundines. None were found. On the twentieth day, a consultant in infectious diseases suggested changing to kanamycin and chloramphenicol and, if this failed, surgical exploration should be considered.

Dr. Kaufman

This brings up some general questions. Dr. Reinfrank, what in your mind is the cause of any fever? It is physiologically useful, and can you tell anything by the type of fever?

Dr. Reinfrank

In many instances, for example, bacterial and viral infections, the fever seems to be due to release of a pyrogen, either from the polymorphonuclear leukocyte or some type of pyrogenic substance from tissue cells. Any systemic disease may produce a disorder of temperature regulation, manifested by flushing, sweating, pallor, or it may be measurable with a thermometer. The common denominator of most fevers is some sort of inflammation. In general, there doesn't seem to be much biological advantage in having a fever, with the concomitant loss of salt and water, and plasma volume contraction. Some argue that a fever is beneficial because the reaction of immune mechanisms is increased, but it is difficult to comprehend how two or three degrees of temperature rise can significantly change enzymatic reactions.

When you try to diagnose disease from fever curves, you are apt to be wrong. Of course, there are said to be certain characteristic fevers: the typhoid type, the sustained fever, the remittent or the intermittent, and so on. The point, I think, is that any agent that can cause fever can cause just about any type of temperature curve. The double spikes used to be considered a manifestation of gonococcal endocarditis or kala-azar. Probably the commonest bacterial cause of double daily spike these days would be miliary tuberculosis. In general, however, you can't draw any significant conclusions about the character of temperature curves.

Dr. Kaufman

Dr. Burchell, on the eleventh day all antibiotics were stopped and heparin was instituted. What was the rationale behind this?

Dr. Burchell

To go back a bit, I think it was wrong not to take a blood culture before antibiotics were started, because a temperature of 103°F is unusual in pyelonephritis without any symptoms of pyelonephritis. So I would have considered bacteremia. Since we expect a good response to antibiotics by the fifth day, this was probably not a urinary tract infection, and the working diagnosis was probably wrong. Now, at this point, if it were a pelvic infection, it was serious and potentially lethal. I think I would pull out all the stops and go to high doses of antibiotics. Again, the patients who died of puerperal sepsis developed peritonitis on the seventh to ninth day. This patient didn't seem to have that complication. Also, this usually responds to antibiotics. However, one entity does not respond well to antibiotics, and that is suppurative pelvic thrombophlebitis. If antibiotics did not produce a good response, then heparin should be started. If that was not helpful one ought to consider surgical therapy. Heparin has not been generally used in this disorder but it seems to be helpful in some patients. I think I would have added heparin without stopping the antibiotics. In retrospect heparin when given just for days 12 to 16, was probably of therapeutic value in this case since the temperature did decrease. Whether the rest of the course would have been altered had she been continued on heparin is open to question.

Dr. Kaufman

Dr. Pyrtek, when does the surgeon consider diagnostic laparotomy?

Dr. Pyrtek

I assume that repeated examinations showed no significant findings in the abdomen. I notice the alkaline phosphatase was measured more than once and rose from 6 to 160. Did you think this was significant or not?

Dr. Nobert

Well, this is why the diaphragms were x-rayed and the liver scan was done.

Dr. Pyrtek

The liver scan was, I assume, of no help. Repeated x-rays of the chest were always normal, never any fluid at the right or left base?

Dr. Jack L. Westcott

The intravenous pyelogram shows slight hydronephrosis on the right and a lesser degree on the left. Seven days postpartum this is not unusual. One interesting finding is air in the uterine cavity which extends into the fallopian tubes. I don't personally ever remember having seen this, even immediately postpartum. This is strongly suggestive of uterine infection. A chest x-ray 10 days after delivery is normal and repeated three days later shows minimal changes in the left chest. The diaphragm on the left is slightly elevated and there are small streaky densities in the midportion of the left lung. Anything seen here would be suspicious of pulmonary emboli. Gall bladder x-ray showed no abnormalities. The x-rays taken all together probably indicate a uterine infection, with suspicions of pulmonary emboli, a subhepatic abscess or a mass in the pelvis.

Dr. Pyrtek

You must compile all the information possible in an FUO. Then, having done all this, there is usually some abnormality which justifies an operation. Most surgeons would consider exploration as the next logical step in an illness that has evolved in this manner. Just because this patient had a baby and then had fever does not exclude another illness not related to her pregnancy. One likes to tidy up everything in a nice neat package and say that this is all due to pregnancy, but it is not necessarily so. In answer to your questions, yes, I would explore at this point.

Dr. Kaufman

Well, an operation was performed and she got better. Dr. Burchell, would you tell us your preoperative diagnosis?

Dr. Burchell

Well, I think the obstetrician's viewpoint is a little less broad and a little easier than the internist's. Going back to Sutton's Law, it is most probable that this patient had a severe infection associated with her delivery. She had a large baby, a small pelvis, a laceration, all of which, statistically, increase the chances of a severe pelvic infection. She had no response to antibiotics—highly unusual if it were puerperal sepsis. You are left then with only one diagnosis: suppurative pelvic thrombophlebitis. Most such cases have been reported from New Orleans. They have used anticoagulants at times, and I think anticoagulants should be used. Antibiotics should be used, and then if the response is inadequate, you should operate. The findings at operation were interesting. The pelvis, uterus, ovaries, and tubes were all normal. The entire pelvis was normal. The upper half of the left ovarian vein was replaced by a hard cord. On the right side just above the ovary the vein was normal. About halfway up, it was thick and indurated, about 1.5-2.0 cm in diameter. The clot and some of the induration extended up to and around the right renal vein. The common iliac veins and the vena cava just after the confluence were palpably normal. Since the clot extended about the renal veins, the vena cava was opened and the clot sucked out from above. This material was white and cheesey in consistency. The indurated segment was completely isolated with sutures.

In my experience, this is a rare complication of pelvic infection. In New Orleans, before the days of antibiotics such cases were operated and the involved vein was tied off, usually one ovarian vein. Some patients improved rapidly, like the present case, and some died. The first cava ligation for this condition was done some twenty years ago, and it was not planned pre-operatively. They found the clot extended up beyond the renal vein. They had never ligated a vena cava for this reason before, but it was considered an infectious process, so the vein was ligated, and the patient recovered. If infected vessels were not ligated, the patients did not get well. This is primarily an infectious process. These patients seldom, if ever, die of pulmonary embolism. Usually they die of the primary process or metastatic abscesses. The only other thing to leave with you is that this started as puerperal infection in the uterus, advancing over the course of three weeks. In the early stages it was an endometritis, then a parametritis, and finally a thrombophlebitis, as a continuing process. It did not begin as a thrombophlebitis of her great veins two weeks before. The temperature of the first week and perhaps part of the second may all have been due to disease in the left ovarian vessel because this cord-like structure must have been infected the earliest. If she had been operated a week and a half earlier, some infection would have been found in the broad ligaments. In my opinion, this was an ever-advancing infection starting in the uterus and at surgery, involving the right ovarian vein and the inferior vena cava.

Dr. Kaufman

In summary, the patient presented fever of obscure etiology which turned out to be secondary to a relatively uncommon disorder: suppurative pelvic thrombophlebitis. The panelists discussed well the general approach to such a problem and clearly described some of the confusion that can develop during the various manipulations in unraveling the problem. They emphasized that appropriate samples for bacteriological culture be systematically collected. A systemized approach to the use of various antibiotics is especially important. Many and varied possibilities were considered in the differential diagnosis, but all discussants seem to emphasize Sutton's Law, that is, look where the money is—in this particular patient, complications of pregnancy.

I wish to thank our discussants for their lucid and in-depth analysis of a difficult clinical situation. Thank you.

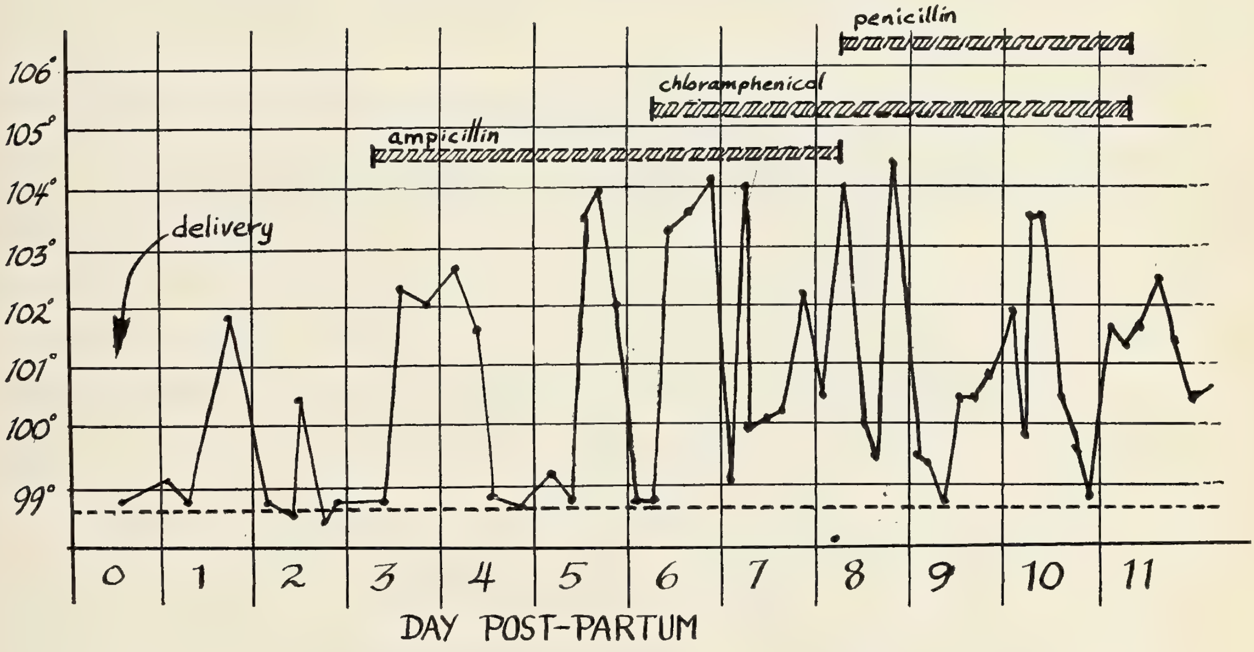
APPENDIX

MISCELLANEOUS LAB TESTS

Heterophile aggultinins	Negative
Heterophile agglutinins	Negative
Febrile agglutinins — Typhoid	Negative
Lipase	Normal
Calcium	4.45 mgm.
Bilirubin	Normal (0.8)
Anti-streptolysin	100 units (normal)
Culture for Tbc from marrow	No growth
Thymol turbidity	1.8 units
Amylase	4
Stool for ova and parasites	None seen
Smear for malaria	Negative
Liver scan	Normal
SGOT	32
SGPT	8
LDH	231-307 u/L
Alkaline phosphatase	62-160 u/L
WBC	6,000-11,700

CULTURE REPORTS

Post Partum Day	*Source*	*Report*
2	Urine	E. Coli 1+
3	Urine	Sterile
5	Blood	Sterile
	Cervix	Sterile
	Episiotomy	E. Coli 1+ Proteus Mirabilus
9	Cervix	Sterile
	Episiotomy	Sterile
12	Lochia	Sterile
13	Bone Marrow	Sterile
15	Urine	Sterile
16	Blood	Sterile
17	Blood	Sterile
18	Urine	Sterile
	Uterus	Sterile
	Uterus	E. Coli 1+
23	Stool	No Pathogens
	Peritoneal Fluid	Sterile



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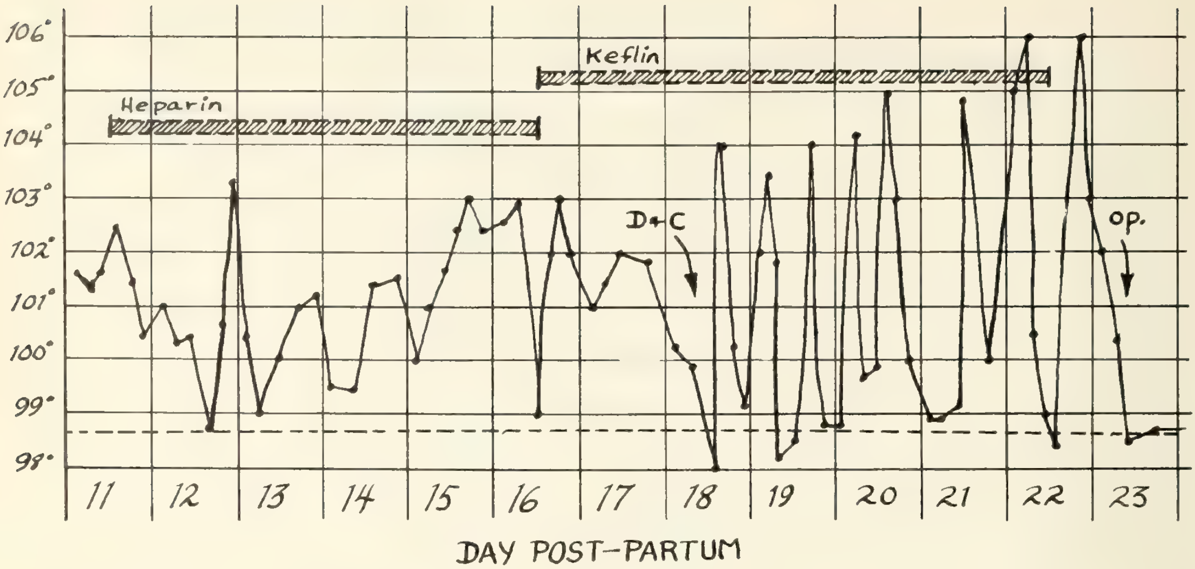

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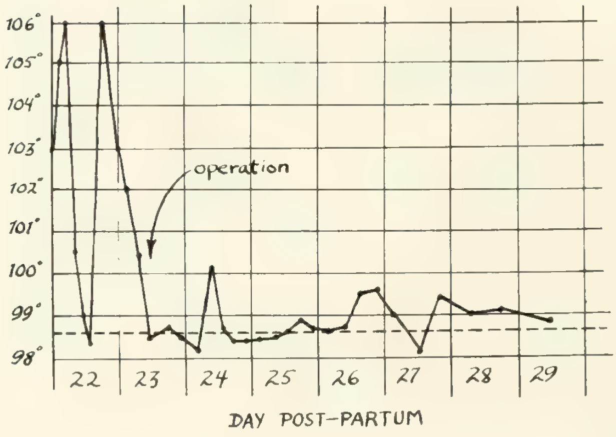

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Assistant to General Manager

SUMMARY OF ACTIONS COUNCIL MEETINGS

Wednesday, August 14, 1968
Wednesday, August 21, 1968
Thursday, August 29, 1968

Foreword

The Council held three consecutive weekly meetings on the dates listed above. From the final hour of the August 14 meeting until the mid-point of the August 29 meeting, the Council was in Executive Session for the purpose of considering and acting upon the items of business indicated in the minutes which follow. For these reasons, the minutes of the three meetings are presented herewith in combined form.

Meeting Of August 14, 1968

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Caplan, Grendon, Weber, Jr., Brandon, Abbot, Fabro, Bradley, Cramer, Farrell, Egan, Petrie, Spitz, Shepard, J. Grant, Nemoitin, Pelz, Granoff and Palomba.

Also present were: Mrs. Lindquist, Mr. Villano, Dr. John W. Patterson, Dr. Frederick C. Redlich, Dr. Franklin M. Foote, Dr. Orvan W. Hess and Dr. Richards.

Absent were: Drs. Gardner, Rogol, Purnell, Johnson, Friedberg, McDonald, R. Grant, Wilson and Roch.

II. Routine Business

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Harry L. Berman New Haven (NHCMA)—1968.
Thomas C. Carey, Hartford (HCMA)—1968.
Patrick T. McIlroy, Bridgeport (FCMA)—1968.
Pauline Riendeau, Old Saybrook (LCMA)—1968.
J. A. Wilson, Meriden (NHCMA)—1968.

III. Old, New and Special Business

Report—Ad Hoc Committee on CRMP Grant Request

Responding to a directive of the Council, this Ad Hoc Committee filed an exhaustive report on its studies of the CRMP Operating Grant Request which was submitted by the CRMP Advisory Board to the National Advisory Council, Division of Regional Medical Programs, National Institutes of Health, on March 1, 1968. As invited guests of the Council, the following members of the CRMP Advisory Board were present and participated fully in the discussion of the Ad Hoc Committee's report: Dr. Frederick C. Redlich, Dean of the Yale University School of Medicine; Commissioner Franklin M. Foote, State Health Department; Dr. John W. Patterson, Dean of the UConn Medical School; and Dr. Orvan W. Hess, New Haven.

Following some four hours of detailed discussion, the Chairman ruled that the Council would go into Executive Session to act upon the report and its recommendations, and all invited guests were excused.

IV. Executive Session, August 14, 1968

Because of the lateness of the hour, it was VOTED to recess the meeting in Executive Session until 1:30 P.M. on Wednesday, August 21, 1968.

Meeting Of August 21, 1968

The recessed meeting in Executive Session of August 14, 1968 was reconvened by the Chairman at 1:45 P.M.

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Caplan, Grendon, Weber, Jr., Brandon, Abbot, Fabro, Bradley, Cramer, Farrell, Petrie, Spitz, Shepard, J. Grant, Johnson, Friedberg, R. Grant, Pelz, Granoff, Palomba and Roch.

Also present were: Mrs. Lindquist and Dr. Richards.

Absent were: Drs. Gardner, Rogol, Egan, Purnell, Nemoitin McDonald and Wilson.

II. Special Business

Following additional general discussion of the report of the Ad Hoc Committee to Study CRMP Operating Grant Request, the Council proceeded to act upon each section of the report with its accompanying recommendation(s) *seriatim*. On each section and each recommendation the Chairman inquired as to whether there was dissenting vote, and, except on two or three minor points, it was determined that the vote was unanimous. At the completion of these deliberations, it was VOTED to accept the report, as amended, and this vote was also confirmed as being unanimous. On the report itself, it was further VOTED to discharge the Ad Hoc Committee with the thanks and commendation of the Council. Pursuant to the acceptance of the report of the Ad Hoc Committee, the following actions were taken:

(1) It was VOTED to apprise by telegram the Director, Division of Regional Medical Programs, National Institutes of Health, that the Council of CSMS was submitting an evaluation of the CRMP Operating Grant Request and urged that the National Advisory Council of RMP not complete its appraisal of the Grant Request until it had received and reviewed the evaluation developed by the CSMS Council. A typed copy of this telegram was mailed to Dr. Clark, CRMP Program Coordinator, the Chairman of the CRMP Advisory Board, and the four members of the Board who were guests at the Council meeting of August 14, 1968.

(2) It was VOTED to direct the staff to prepare forthwith and mail to the National Advisory Council to RMP's a copy of the Ad Hoc Committee's report, as accepted, a "summary statement" on the CRMP Grant Request, and a suitable letter of transmittal and explanation. Members of the Council have since received duplicate copies of the "package" that was mailed in accordance with this action. Duplicate copies were also mailed promptly to all persons listed (under (1)) to receive copies of the telegram.

Upon completing these actions, the hour being late, it was VOTED to again recess the Executive Session until 2:00 P.M. on Thursday, August 29, 1968. By agreement, the first items of business to be taken up at the next meeting are to be a CRMP document titled "Revised Organizational and Operating Structure", which outlines a proposal to enlarge the CRMP Advisory Board, and a request from CRMP for the Council to nominate four CSMS members to serve on said enlarged Board.

Meeting Of August 29, 1968

The recessed Executive Session meeting of August 21, 1968 was reconvened by the Chairman at 2:15 P.M.

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Caplan, Grendon, Weber, Jr., Brandon, Abbot, Fabro, Bradley, Rogol, Cramer, Egan, Shepard, J. Grant, R. Grant, Pelz and Granoff.

Also present were: Mrs. Lindquist, Mr. Villano and Dr. Richards. Dr. Orvan W. Hess joined the Council following return to Regular Session from Executive Session.

Absent were: Drs. Gardner, Farrell, Petrie, Spitz, Purnell, Nemoitin, McDonald, Johnson, Friedberg, Wilson, Palomba and Roch.

CRMP "Revised Organizational and Operating Structure"

Following review of that section of the CRMP proposal to expand the Advisory Board which pertained to number of Board members allocated to the Society (four), it was VOTED to inform CRMP that the Council finds this proposal not to be in accord with the pertinent position adopted by the Council on August 21, 1968; i.e., that the Society "insist on being made an equal partner to the University Deans and Medical Centers in the CRMP structure, and that at least one-third of the Advisory Board be made up of representatives formally designated by the Society", and, further, that the Society "should also have equivalent representation on the Executive Committee (of the Advisory Board)".

Pursuant to this action, it was further VOTED to request the Chairman to appoint an Ad Hoc Committee to study the CRMP document on proposed revision of its structure, and to make a report with recommendations to the next meeting of the Council. Dr. Martin appointed the Ad Hoc Committee as follows: Carl W. Johnson, Thompsonville, Chairman, Frank K. Abbot, Waterbury, Louis Rogol, Danbury, and E. Tremain Bradley, Norwalk.

Taking up the final item of CRMP business, it was VOTED that, in the light of the foregoing, no nominations for service with the CRMP Advisory Board be made at this time.

Having completed action on the report of the Ad Hoc Committee to Study CRMP Operating Grant Request, and other matters concerning CRMP, it was VOTED to adjourn Executive Session and to return to regular Open Session.

Regular Meeting

Report—Committee on Third Party Payments

Actions were taken on several parts of a report filed by this Committee as follows:

(a) *Inadequacies of Blue Cross-CMS Coverage:* It was VOTED to receive as information the report of the Committee on the complaints of an NHCMA member concerning inadequacies in Blue Cross-Blue Shield coverage with regard to procedures possible of rendering on an

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Warning: This drug is an analog of phenylbutazone; sensitive patients may be cross-reactive. If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Persistent or severe dyspepsia may indicate peptic ulcer; perform upper gastrointestinal x-ray diagnostic tests if drug is continued. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with caution in the first trimester of pregnancy, and in patients with thyroid disease.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patients should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia), sudden weight gain (water retention), skin reactions, black or tarry stools or other evidence of intestinal hemorrhage occur. Make complete blood counts at weekly intervals during early therapy and at 2-week intervals thereafter. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The more common are nausea and edema. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension, the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately after meals or with milk to minimize gastric upset. Drug rash occasionally occurs. If it does, promptly discontinue the drug. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), or a generalized allergic reaction similar to a serum sickness syndrome may occur and require permanent withdrawal of medication. Agranulocytosis can occur suddenly in spite of regular, repeated normal white counts. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, hypersensitivity angiitis, pericarditis and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur

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outpatient basis but which presently require hospital admission in order to be qualified for benefits. While it was felt that the new Blue Cross coverage of pre-admission testing constitutes a step in the right direction, it was VOTED to request the Committee on Third Party Payments to study ways and means of achieving better third party coverage of all types of outpatient services without giving encouragement to hospitals to move further into the business of providing physicians services as well as hospital services.

(b) *Updating the Relative Value Schedule:* In response to the Committee's request for direction in proceeding with its assigned task of updating the RVS, it was VOTED to ask the General Manager to remind the Committee that the Society has no interest in dollar conversion factors at this time, and that the sole objective of this assignment is to obtain from CSMS Sections and allied groups recommendations for changes in the RVS as it was adopted in 1965; i.e., changes in the unit values of listed procedures, deletions of outmoded procedures, additions of new procedures not now listed, etc. It was further VOTED to authorize the Committee to attempt to compromise equitably differing recommendations received from related sections and groups (Example: Pediatrics, Internal Medicine and General Practice).

(c) *Statements re Group Practice:* It was VOTED to approve two statements recommended by the Committee as follows:

  (1) That CSMS approve only those groups in which practicing physicians have policy control in matters having to do with the delivery of health care.

  (2) That CSMS approve only such groups as guarantee free choice of physicians by patients.

Nominations to Connecticut Advisory School Health Council

It was VOTED to nominate to succeed themselves for two-year terms as Delegates to the CASHC the following members: Joseph J. Bellizzi, Hartford; Louis A. Parrella, North Haven. The terms run from May, 1968 to May 1970.

Report—Committee on National Legislation

Proposed Legislative Conference: It was VOTED to approve a proposal submitted by the Committee to arrange a legislative conference in the fall for Council members, legislative committee members, county medical association officers and others who are interested. The Council recommends that the format for the Conference of County Medical Association Officers be utilized for this purpose. In approving the proposal, the Council requests the Committee prepare and submit to the Council an outline of the legislative conference to be held, with cost estimates for same.

Report—AMA Delegate

It was VOTED to accept, with thank and commendation, the report submitted by Max Caplan, AMA Delegate, on the proceedings of the meeting of the AMA House of Delegates, San Francisco, June 16-20, 1968. It was further VOTED to have published in the Journal the AMA policy statement on chiropractic, this action to be taken in accordance with the recommendation of the AMA House of Delegates that the state medical societies "alert public (and the medical profession) of the health hazard posed by the cult of chiropractic".

Finally, it was VOTED to request the Ad Hoc Committee on Medical Quackery to study the problems posed by chiropractors in Connecticut, past and present, and to make recommendations concerning same to the Council.

It was also VOTED to refer to the Committee on Hospitals, for study and report, the question of how more physicians may become voting members of hospital governing bodies.

Progress Report—Release of Medicaid Information

Reporting for Dr. Gardner, in the latter's absence, the General Manager informed the Council that the CSMS legal counsel had reviewed the "right to know" statutes in relation to the possible release of Medicaid information (including the names of physicians and the amounts of Title XIX payments received) to the communications media. In brief, counsel's opinion was that the Welfare Commissioner would be obliged to release only such information, and in such form, as would not jeopardize "efficient administration" of the program (as provided for in P.L. 89-97). At a meeting with Commissioner Shapiro and Dr. Hess, Drs. Gardner and Richards and Mr. Villano, the statistics concerning Medicaid payments for the period now reportable (through December 31, 1967) were reviewed and it was concluded that the statistics were quite favorable in the areas of physician participation and medical service disbursements. The General Manager also reported that the Attorney General's office has not yet made a final ruling in this matter. Dr. Hess, Welfare Medical Director, a guest at the Council meeting, confirmed the major points of this progress report and indicated that an effort would be made by the Department and the Society jointly to publicize the valuable contributions which have been made by the Society and many of its members toward making the Medicaid program more meaningful to beneficiaries and assisting the Department in administering the "usual and customary charge" method (since March 1, 1968) on a fiscally sound basis. It was VOTED to receive these reports as information and to take no further action concerning the release of Medicaid information at the present time. It was further VOTED to ask the members of the Title XIX Medical Advisory Committee who sit on the Council to constitute a liaison committee with the State Department of Welfare. A complete roster of such members will be compiled.

Nominations—Drug Advisory Council

It was VOTED to receive as information, and with thanks for services rendered, the decision of Eric E. Stietzel, Norwalk, to terminate his membership (appointed by the Governor) on the Drug Advisory Council (established by the 1967 General Assembly). It was further VOTED to submit the names of the following CSMS members to Governor Dempsey for his selection of a physician to replace Dr. Stietzel on the DAC: Frank K. Abbot, Waterbury; Max Caplan, Meriden; and Benjamin Wiesel, Hartford.

Date of Next Meeting

Although several additional items of miscellaneous business were discussed informally, it was determined that a quorum was no longer present and the meeting was adjourned without further actions being taken. The next meeting is scheduled for Wednesday, September 25, 1968, starting at 2:00 P.M.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on August 14, 21 and 29, 1968. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

PEDIATRICIAN—32 years of age, Board eligible with National Boards. Wishes to establish himself with a group or associate practice about September or October 1968. Presently completing military obligations.

INTERNIST—Board eligible with cardiology subspecialty; 14 years private practice in Connecticut, also administrative and teaching experience. Will consider group, hospital or industrial position; clinical or administrative.

INTERNIST—41 year old internist-cardiologist seeks association with group, industry or institution. Has specialty training, also, in chest diseases and dermatology. Connecticut license.

INTERNIST—Board certified with subspecialty of hematology, wishes to practice in a hospital, in laboratory work and patient care. Would like at least part or full-time hospital practice. Has National Boards and is available in October, 1968.

ANATOMIC PATHOLOGIST—Board eligible with Connecticut license would like to practice with an associate. Available immediately, 32 years of age.

PATHOLOGIST—34 years of age, Board certified, has applied for Connecticut license. Would like to practice in a hospital or in private practice. Available as of November 1, 1968.

Placement Opportunities

CONNECTICUT—NEWINGTON — Psychiatrist, full-time or part-time, for expanding multidisciplinary psychiatric service of General Hospital. Salary dependent upon qualifications. Liberal fringe benefits. Write: A. Ioannides, M.D., Acting Chief, Psychiatry Service, VA Hospital, Newington, Connecticut 06111.

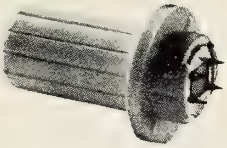
PART-TIME PHYSICIANS—Tours of duty are available to provide coverage on our Intermediate (Extended Care) Service, evenings, nights and weekends. For example, 5:00 P.M.-8:00 A.M. (Weekdays) $69.60 per tour; or 8:00 A.M.-8.00 P.M. (24 hrs. Sat. or Sun.) $111.36 per tour. Interested physicians may make arrangements for intermittent or varying part-time hours of duty provided acceptable coveage is maintained during these periods. Part-time salary will be pro-rated according to above rates. Physicians must be U.S. citizen or possess permanent visas, and have licensure in one of the States. Write, visit or telephone: Personnel Officer or Chief of Staff, Veterans Administration Hospital; West Spring Street; West Haven, Connecticut 06516.

SENIOR PHYSICIAN—Openings for Senior Staff Physician—$16,370-$19,970. Many liberal benefits.

Tuberculosis? Influenza?
Pneumonia? Leukemia?
Hodgkin's Disease? Syphilis?
Systemic Fungal Diseases?
Chronic Chest Diseases?
or

HISTO?

(Histoplasmosis—"The Masquerader")



A new aid in differential diagnosis

HISTOPLASMIN, TINE TEST
(Rosenthal)

The LEDERTINE™ Applicator with the Blue Handle

Precautions—Nonspecific reactions are rare, but may occur. Vesiculation, ulceration or necrosis may occur at test site in highly sensitive persons. The test should be used with caution in patients known to be allergic to acacia, or to thimerosal (or other mercurial compounds).

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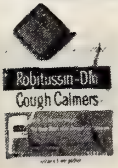
Ask your representative for details or write Medical Advisory Dept.,
Lederle Laboratories, Pearl River, New York 10965. 406-8

BETTMAN ARCHIVE
Gotta make a pit stop to take my cough syrup.
Full speed ahead, Fred. These solid Cough Calmers can control that cough for 6 to 8 hours.
2



Each Cough Calmer™ contains the same active ingredients as a half-teaspoonful of Robitussin-DM®: Glyceryl guaiacolate, 50 mg.; Dextromethorphan hydrobromide, 7.5 mg. A. H. Robins Company, Richmond, Virginia 23220

A-H-ROBINS

Teething is easier

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DENTOCAIN MILD

Easier on the Baby . . . Dentocain Mild makes it easier to go through the troublesome teething period. A small amount, applied with gentle massage, brings quick, soothing relief to irritated and inflamed gum tissue; aids in getting infant back to sleep.

Easier on the Mother . . . by providing more comfort and extra sleep for the baby, Dentocain Mild grants the mother greater peace of mind and several additional hours of necessary rest.

DENTOCAIN ADULT is also useful in providing temporary relief for pain of adult toothache. (Adult Formula contains 20% Benzocaine.)

FORMULA

Alcohol 70%
Bencocaine 10%
Chloroform, 4 mins. per fluidounce

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Bloomfield, Conn. 06002

Professional samples and descriptive literature sent on request.

Live-in at minimal cost. Write Veterans Home and Hospital, Rocky Hill, Connecticut or call 529-3571, Ext. 395.

HOUSE PHYSICIAN—FULL TIME—to cover Emergency Room and house calls. Night coverage, five nights a week, 6 P.M. to 7 A.M. Must have Connecticut license. $20,000 a year with apartment; good fringe benefits. Minimum contract one year. Write P.O. Box 3494, Bridgeport, Connecticut 06604.

CONNECTICUT—PSYCHIATRIST, CHIEF OF PROFESSIONAL SERVICES needed for a community-oriented decentralized mental hospital; will develop, direct and coordinate all clinical services in 1600-bed hospital; review and modify operating criteria for standards of service; coordinate clinical treatment, training and research activities; OPD, day-care, in-patient, consultation and emergency services included; opportunity for association with Wesleyan and Yale Universities and UConn. Starting salary commensurate with training and experience; liberal fringe benefits. All particulars should be sent in first letter to M. K. Arafeh, M.D., Superintendent; Connecticut Valley Hospital; Box 351, Middletown, Connecticut 06457.

ANESTHESIOLOGIST—to associate with another anesthesiologist at the World War II Veterans Memorial Hospital, Meriden, Connecticut. For further information, contact Marvin Albert, M.D. World War II Veterans' Memorial Hospital, Paddock Avenue, Meriden, Connecticut 06450 or telephone 237-5531.

G.P.—Terminating large general practice of 30 years on October 1, 1968, to assume Emergency Room duties at the New Britain General Hospital. Interested in finding physician to take over practice. Contact immediately: Roger T. Scully, M.D., 55 West Main Street, New Britain, Connecticut 06051, Phone (203) 223-0251.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

The American Academy Of Clinical Toxicology

The American Academy of Clinical Toxicology has been founded for the advancement of clinical toxicology, a medical specialty concerned with the diagnosis and treatment of poisoning and drug intoxication.

The purposes of the Academy are to encourage clinical investigation, to promote the development of diagnostic and therapeutic methods, to foster among practicing physicians a better understanding of the treatment of poisoning, and to improve the medical care received by the poisoned patient.

Five catagories of membership are provided. *Fellowship:* Fellows are physicians in the full time practice of clinical toxicology with five years experience and who have been judged by the Examining Committee to have fulfilled the requirements set forth by the Constitution and By-laws. *Active Members:* Physicians who are called upon to provide clinical care for the poisoned patient as part of their practice. *Associate Members:* Physicians with no direct involvement in patient care and other scientist whose activities contribute to the advancement of clinical toxicology. *Honorary:* Honorary membership may be voted non-members in recognition of distinguished service or contributions to the objectives of the Academy. *Sustaining Members:* Sustaining membership is provided for organizations wishing to contribute additional financial support to the Academy as an aid in the achievement of its objectives.

The Academy will provide its members with a suitable periodical for the publication of original contributions to clinical toxicology. In addition to an annual business meeting and scientific program, the Academy will sponsor a symposium on some aspect of the practice of clinical toxicology with the proceedings to be distributed to the membership. Ad Hoc committees will be appointed by the Academy to prepare special reports intended to assist the physician toward better utilization of available resources. Subjects under consideration are: Emergency room facilities, ER and I.C.U. nursing, Rapid analytical procedures, Documentation and reporting of toxic reactions, etc. *Clinical Guidelines* in the treatment of poisoning will be a series of brief discussions limited to individual toxic substances presenting pertinent data required for clinical management. The Academy will maintain a register of consulting clinical toxicologists.

WOMAN'S AUXILIARY

President
Mrs. Clarence W. Harwood, Middletown

President-Elect
Mrs. James F. Jones, Danielson

First Vice-President
Mrs. Nicholas A. Marinaro, Newington

Second Vice-President
Mrs. John J. Mendillo, Hamden

WOMAN'S AUXILIARY CONNECTICUT STATE MEDICAL SOCIETY

Recording Secretary
Mrs. Melville Y. Alderman, West Hartford

Corresponding Secretary
Mrs. Donald E. Miller, Middletown

Treasurer
Mrs. Edwin R. Connors, Hartford

THE YEAR AHEAD

The President of the Woman's Auxiliary to the American Medical Association, Mrs. C. C. Long of Arkansas, has put the accent on youth for the coming year. In her inaugural address she stated that the "youth of the country hold the key to tomorrow". "Doctors' wives are one of the few groups that can enlighten the public to the true medical and health situation in our country today. We have many helpful programs, not only for our young people, but for the good of all people."

The auxiliary programs to be stressed this year are as follows:

1. AMA-ERF—We need to help educate more doctors and to advance our knowledge of medicine.
2. Health Careers—More young people must be given information about the many careers open to them in the medical field to increase the number of available workers.
3. Legislation—This is the year to get out and vote and to work on the election in some way.
4. Community Health—Learn your community's health resources and work for their improvement.
5. Home-centered Health Care and Rural Health.

"Package Programs" are available to county auxiliaries for presentation where there is a need. All are "youth accented" in line with the national president's plans for the year. A package program is a health education presentation developed by the AMA Auxiliary to help the county auxiliary focus public attention on an urgent health need. The national auxiliary can only suggest programs and offer assistance in promoting them. The success of any of these depends upon the state and, most importantly, the county efforts to work effectively to carry them out.

The seven programs available are as follows:

Teenage Venereal Disease. The folio gives you information for 2 auxiliary programs. One is for adult representatives of community public and voluntary agencies. The other is for youth or school groups. Films and pamphlets are used in the presentation.

Youth Health and Fitness. Complete information and material for stimulating community understanding of the value of health education in the physical, mental and social wellbeing of youth. Film and pamphlets.

Mental Health of Children. Information for a program designed to stimulate concern for the emotional well-being of children. Film and take-home booklets.

Health Careers. Information for the presentation of 2 auxiliary sponsored programs to bring to public attention the need for professional, trained, and skilled personnel in health careers and allied services. Package "A" for adults; "B" for students. Slide program and take home booklets.

Immunization. Materials designed to bring to public attention individual and community responsibilities in communicable disease control. Film and pamphlets.

The Block Mother Plan. Designed to interest PTAs and other groups in setting up a system to protect children going to and from school.

Homemaker Service. Material for an auxiliary-sponsored presentation in communities where there are at present no homemaker services, but where there is an apparent need for one. Film and booklets.

For some months we have known that the national auxiliary would present at the annual convention an amendment to the Bylaws regarding an increase in dues. Increased costs of material and labor and a diminishing reserve fund which can no longer be drawn upon forced the amendment. This amendment was passed unanimously and beginning with the collection of dues after June 30, 1969 national will be paid $4 for each member instead of the previous $2. A subscription to *MD's Wife* will, of course, be included in the dues payment.

REMEMBER – – –

October 21—Auxiliary Workshop—Training session for all county officers and chairmen.

November 5—Election Day.

AROUND THE STATE

New Haven County

BOARD OF GOVERNORS

New Haven County Medical Association
August 22, 1968

A meeting of the Board of Governors of the New Haven County Medical Association was held at the Colonial House, Hamden, Conn., on August 22, 1968.

Following routine business reports from Ad Hoc Committees were taken up.

Our Senior Councilor, Dr. Stuart Petrie, brought us up to date on the last two Council meetings in which matters sent up by New Haven County were disposed of. One of these was a complaint by one of our doctors about his treatment by a presiding judge who criticized the doctor's fees publicly, even though these fees were lower than usual and customary. This matter was referred to the Bar Committee of the Connecticut State Medical Society. A large part of the Council meeting had to do with latest on the Connecticut Regional Medical Plan. Our member, Dr. Frank Abbot, acting as Chairman, rendered an excellent report which could have later repercussions.

The meeting closed after a lengthy summary of Ad Hoc Committees by our President, Dr. Charles Verstandig.

Dr. Kurt Pelz was commended for his work to date on the Fair Haven Project and on his efforts as Chairman of the Third Party Review Committee.

There will be a further report on the Project in Fair Haven to supply medical assistance by volunteer doctors from our County.

The meeting closed with a social hour and dinner.

Respectfully submitted,
H. A. LEVIN, M.D. Clerk

Q. How much does the **anticostive*** **hematinic** cost?

A. No more than costive hematinics cost!

The anticostive hematinic is
PERITINIC®
Hematinic with Vitamins and Fecal Softener

A tablet-a-day provides:

● Elemental Iron (as Ferrous Fumarate)	100 mg
● Dioctyl Sodium Sulfosuccinate (to counteract constipating effect of iron)	100 mg
Vitamin B_1	7.5 mg
Vitamin B_2	7.5 mg
Vitamin B_6	7.5 mg
Vitamin B_{12}	50 mcgm
Vitamin C	200 mg
Niacinamide	30 mg
Folic Acid	0.05 mg
Pantothenic Acid	15 mg

Bottles of 60

*

anticostive, *adj.* (*anti* opposed to + *costive* causing constipation.) Against constipation. (Now isn't that a good idea in an iron-containing hematinic? We'll send you samples if you'll send a request on your Rx blank, addressed to Department 150.)

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pileptic patients...
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DILANTIN is useful in the treatment of grand mal epilepsy and certain other convulsive states. Its use will prevent or greatly reduce the incidence and severity of convulsive seizures in a substantial percentage of epileptic patients, without the hypnotic and narcotizing effects of many anticonvulsant drugs.
PRECAUTIONS: Periodic examination of the blood is advisable. Nystagmus in combination with diplopia and ataxia indicates dosage should be reduced. The possibility of toxic effects during pregnancy has not been explored. ADVERSE REACTIONS: Allergic phenomena such as polyarthropathy, fever, skin eruptions, and acute generalized morbilliform eruptions with or without fever. Rarely, dermatitis goes on to exfoliation with hepatitis, and further dosage is contraindicated. Gingival hypertrophy, hirsutism, and excessive motor activity are occasionally encountered. During initial treatment, side effects may include gastric distress, nausea, weight loss, nervousness, sleeplessness, feeling of unsteadiness. Macrocytosis, megaloblastic anemia, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, agranulocytosis, and aplastic anemia have been reported. Nystagmus, lymphadenopathy, lupus erythematosus, erythema multiforme (Stevens-Johnson syndrome), and a syndrome resembling infectious mononucleosis with jaundice have occurred.
DILANTIN is supplied in several forms including Kapseals® containing 0.1 Gm. and 0.03 Gm. diphenylhydantoin sodium.
Parke, Davis & Company, Detroit, Michigan 48232

The color combinations of the banded capsules are Parke-Davis trademarks. The orange-banded white capsule identifies Parke-Davis 0.1 Gm. diphenylhydantoin sodium; the pink-banded white capsule 0.03 Gm. diphenylhydantoin sodium.

PARKE-DAVIS 015R67

OBITUARIES

Hartwell Greene Thompson, M.D.
1892-1968

"Tommy" Thompson boasted a proud New England heritage. He was born in Taftville, Conn. in 1892. His father, a "primary physician" stimulated a love for the practice of medicine in Tommy at an early age; and he devoted his life to living up to this ideal. His forebears came from Maine.

He graduated from Norwich Free Academy in 1909, from Yale University in 1913, and from Harvard Medical School in 1917. He interned at Hartford Hospital and served under Colonel Patton (later the well-known General) in the Tank Corps in France in World War I.

His preceptor in obstetrics-gynecology was Hartford's first obstetrician, Dr. T. Weston Chester. He practised this specialty 41 years until ill health brought about his retirement in 1961.

He was appointed to the staff of Hartford Hospital in 1923, and was senior obstetrician and gynecologist from 1934 to 1955 at which time he became a member of the honorary staff. During this time he served as chief of the Department of Obstetrics and Gynecology; chairman of the executive committee and president of the Staff. He was a member of the Consulting Staff of several central Connecticut hospitals.

He was a member of the American Medical Association, the Connecticut State Medical Society, the Hartford County Medical Association, the Hartford Medical Society, the American College of Surgeons, the New England Obstetrical and Gynecological Society, and a founder of the Knife and Stork Club, and of the Connecticut Society of American Board Obstetricians and Gynecologists.

He is survived by his wife Sigrid Johnson Thompson, two sons, Dr. Hartwell Greene Thompson, Jr., Professor of Neurology, University of West Virginia Medical School, and author George Selden (Thompson) of New York City; a sister, Miss Helen G. Thompson and four grandchildren.

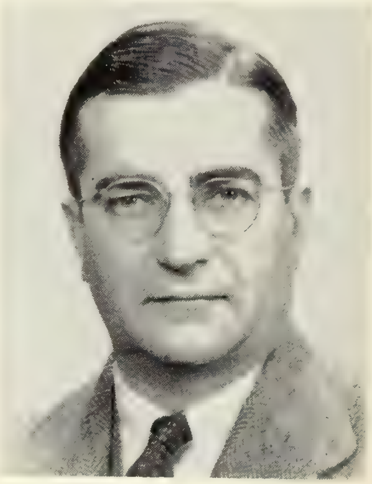
He succumbed to primary lateral sclerosis after a long and distressing illness.

"Tommy" Thompson endeared himself to many people both in and out of the profession. The Hartwell G. Thompson Fund of Hartford Hospital has been generously subscribed by his admiring patients. He was a forceful individual with many interests, an avid student of Americana, an educator of younger physicians, a raconteur, and a baseball buff. His memory will long endure in the hearts of those who knew him.

Louis F. Middlebrook, M.D.

William Sidney Perham, M.D.
1905-1968

William Sidney Perham, M.D., Chief of the Orthopedic Section of the Hospital of St. Raphael in New Haven, died August 1, 1968. So far as any of his associates could tell he was in good health until March 28th, when he suddenly came down with a heart attack and was taken from his home in Woodbridge to the intensive care unit of Yale-New Haven Hospital. Here, four months and four days later, he was to die. A brief mercy eased the final chapter of his life; he was able, for a time, to return to his home. During this interval he must



have amply sensed, in the visits of numerous friends, the admiration and deep affection in which he was universally held.

In addition to his position at St. Raphael's, Sid served as Associate Clinical Professor of Orthopedic Surgery at Yale and Chief Orthopedic Surgeon of its Department of University Health. Diplomate of the American Board of Orthopedic Surgery, he was an attending at Yale-New Haven Hospital and during World War II orthopedic chief of its overseas affiliate, the 39th General Hospital. His memberships in professional organizations included the American Medical Association, American Academy of Orthopedic Surgeons and the Connecticut State Medical Society. Following an extended term as secretary-treasurer of the Society's Orthopedic Section he served for a year as president of the Section.

Sid was appointed Chief of the Orthopedic Section at St. Raphael's in January 1956. Much had to be done to move the Section into mainstream orthopedics, and perhaps he knew the job would take the rest of his life. Most of the work and all the frustrations he reserved for himself. He spent more time at St. Raphael's than in his own practice. Still, there was always time for you, whoever you might be. In the end he finished what he had set out to do. The educational base of the Section was strengthened and extended to a full four years of Board-accredited training. The attending staff evolved from a list of names into a strong, lively service, all without a single directive from their chief. Today the Section stands as tribute and memorial of Sid Perham, to his unending patience, to his consummate skill in handling people and their all but unvarying response to him in terms of respect and loyalty.

In the ease and spaciousness of his nature Sid seemed to reflect the Maine where he had been born, the wilderness of stream and shore to which he loved to return. His unique warmth, his tolerance, his amazing recall of all he had experienced—perhaps these help a little in understanding why he knew so much of friendship, so little of enemity. His modesty, in an age of self-projection and the image, made him an anachronistic delight. Superbly knowledgable as an orthopedic surgeon, to his patients he was the supreme doctor. Above and beyond his surgical skill he was a compassionate physician and serene spirit. Few of us may hope to reach as closely as he did to the ideal physician.

Sid is survived by his wife Helen, his mother, two sons and two daughters; and by six grandchildren.

R.V.F.

In Memoriam

McMahon, William H.—East Norwalk; Fordham Medical School, 1920. Dr. McMahon had practiced surgery in East Norwalk for over twenty years. He was a Fellow of the American College of Surgeons and a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. McMahon died September 1, at the age of 73.

Strayer, Estella—Stratford; Columbia College of Physicians and Surgeons, 1933. Dr. Strayer was a practicing obstetrician and gynecologist in the Stratford area for 34 years. During 1952-53, she served as deputy Chief Medical Officer for the Pentagon. She was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Strayer died August 10, at the age of 66.

Genetic Services Directory Issued

A new publication, *International Directory of Genetic Services,* has been compiled by a Creighton U. School of Medicine official and the director of the National Foundation-March of Dimes medical department.

Henry T. Lynch, M.D., chairman of the Dept. of Preventive Medicine and Public Health at Creighton, is co-editor of the publication with Daniel Bergsma, M.D.

Dr. Lynch said the directory is designed to provide medical and basic science researchers with information that relates to medical genetic studies conducted by researchers engaged in the study of hereditary diseases.

He said the genetics directory carries a coded breakdown of 23 genetic services, including birth defects, population genetics, cancer genetics and social service.

WHEN YOU MOVE — LET US KNOW!
WE WANT YOU TO BE SURE TO GET
THE NEXT ISSUE OF
CONNECTICUT MEDICINE

This advertisement for TAO® (triacetyloleandomycin), published at the request of the Food and Drug Administration, replaces a recent one which the FDA regards as misleading.

The advertisement headlined "new evidence for TAO . . ." and emphasized that the drug is "for the frequently seen respiratory infection in the office and for a problem pathogen* in the hospital. *Staphylococcus aureus."

We emphasize that triacetyloleandomycin is to be used only for acute, severe bacterial infections where adequate sensitivity testing has demonstrated susceptibility to this drug and resistance to other less toxic agents. In view of the possible, but reversible, jaundice and hepatotoxicity of this drug, other less toxic agents should be used unless the organism is resistant to those agents, or in those cases where hypersensitivity precludes their use.

TAO is contraindicated in pre-existing liver disease or dysfunction, and in individuals who have shown hypersensitivity to the drug.

The advertisement emphasized that no tooth staining has been reported after ten years of use of this antibiotic. The Food and Drug Administration regards this claim as an implied comparison suggesting that triacetyloleandomycin and tetracycline have a similar antibacterial spectrum of effectiveness, and that TAO has less toxic potential. Any such implication is not intended and, of course, would be invalid.

The advertisement referred to a research study in which patients were given triacetyloleandomycin prior to determining the susceptibility of the offending organism. Any suggestion that triacetyloleandomycin be used clinically without first determining susceptibility of the offending organism should be disregarded.

ROERIG Rx

J. B. ROERIG DIVISION
CHAS. PFIZER & CO., INC.
235 EAST 42nd STREET
NEW YORK, N.Y. 10017

TAO®(triacetyloleandomycin)
Brief Summary

INDICATIONS: Include streptococci, staphylococci, pneumococci and gonococci. Recommended for acute, severe infections where adequate sensitivity testing has demonstrated susceptibility to this antibiotic and resistance to less toxic agents.

CONTRAINDICATIONS: Contraindicated in pre-existing liver disease or dysfunction, and in individuals hypersensitive to the drug.

PRECAUTIONS: CAUTION: USE OF THIS DRUG MAY PRODUCE ALTERATIONS IN LIVER FUNCTION TESTS AND JAUNDICE. CLINICAL EXPERIENCE AVAILABLE THUS FAR INDICATES THAT THESE LIVER CHANGES WERE REVERSIBLE FOLLOWING DISCONTINUATION OF THE DRUG.

Not recommended for prophylaxis or in the treatment of infectious processes, which may require more than ten days continuous therapy. In view of the possible hepatotoxicity of this drug when therapy beyond ten days proves necessary, other less toxic agents should be used. If clinical judgment dictates continuation of therapy for longer periods, serial monitoring of liver profile is recommended, and the drug should be discontinued at the first evidence of any form of liver abnormality. When treating gonorrhea in which lesions of primary or secondary syphilis are suspected, proper diagnostic procedures, including dark-field examinations, should be followed. In other cases in which concomitant syphilis is suspected, monthly serological tests should be made for at least four months. When used in streptococcal infections, therapy should be continued for ten days to prevent the development of rheumatic fever or glomerulonephritis. The use of antibiotics may occasionally permit overgrowth of nonsusceptible organisms. A resistant infection or superinfection requires reevaluation of the patient's therapy. In the event such occurs with this drug the medication should be discontinued, and specific antibacterial and supportive therapy instituted.

ADVERSE REACTIONS: Although reactions of an allergic nature are infrequent and seldom severe, those of the anaphylactoid type have occurred on rare occasions.

ROERIG
J. B. ROERIG DIVISION
CHAS. PFIZER & CO., INC.
235 EAST 42nd STREET
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BETTMAN ARCHIVE

Just one tablet at bedtime • Prevents painful night leg cramps • Permits restful sleep

How many of your patients stamp their feet at night and lose sleep because of painful leg cramps? Unless prompted, they usually fail to report this distressing condition and suffer needlessly.

One tablet of QUINAMM at bedtime usually controls distressing night cramps and permits restful sleep with the initial dose.

Prescribing information—Composition: Each white, beveled, compressed tablet contains: Quinine sulfate, 260 mg., Aminophylline, 195 mg. **Indications:** For the prevention and treatment of nocturnal and recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis and static foot deformities. **Contraindications:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Side Effects/Precautions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets.

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144

MEETINGS

BASIC SCIENCE

Recent Advances in Clinical Physiology

Tuesdays, 7:15 P.M., through June 10, 1969

Lawrence and Memorial Hospitals Auditorium, New London

Seventh series of courses (20) in basic science as related to clinical medicine; participants granted 40 hours of post-graduate credit by the Connecticut Academy of General Practice. Registration limited to 75; fee $100 for the 20 seminars. Director, Edward Gipstein, M.D., Director of Medical Education, Lawrence and Memorial Hospitals and Chief, Department of Medicine. Co-Director, Richard Gorlin, M.D., Senior in Medicine and Director of Cardiovascular Research, Peter Bent Brigham Hospital, Boston. Speakers from Peter Bent Brigham Hospital and Harvard Medical School.

MEDICINE

November 15 9:00 A.M. - 5:00 P.M.

Symposium on Perinatal Mortality

Connecticut General Life Insurance Company Building, 900 Cottage Grove Road, Bloomfield

Sponsored by the Committee on Perinatal Mortality, Connecticut State Medical Society; Connecticut State Health Department, Yale University School of Medicine

Participants: Moderator, Mary Ellen Avery, M.D., Associate Professor of Pediatrics, Johns Hopkins Hospital, Baltimore; Guest Lecturers, John W. Greene, Jr. M.D., Lexington, Kentucky; Kurt Hirschorn, M.D., Professor of Pediatrics, Mt. Sinai, School of Medicine, New York City; Fritz Fuchs, M.D., Professor of Obstetrics and Gynecology, Cornell University Medical School, New York City; Louis Gluck, M.D., Professor of Pediatrics, University of Miami School of Medicine; Philip Sarrel, M.D., U.S. Army, while at Yale University, Director of the Unwed Mothers Program; Bradley E. Smith, M.D., Associate Professor of Anesthesiology, University of Miami School of Medicine; and Milton Markowitz, M.D., Associate Professor of Pediatrics, John Hopkins Hospital, and Professor-Chairman of Department of Pediatrics, University of Connecticut Medical School, beginning July 1, 1969.

Luncheon available on premises.

PSYCHIATRY

Fall series underway

Psychiatry for Non-Psychiatric Physicians

Case centered seminars with up to 10 practitioners per group. Eight to 10 weekly sessions at locations around the state.

Sponsored by the Connecticut Academy of General Practice and the Connecticut Branch of the American Psychiatric Association.

Contact: Stephen Fleck, M.D., Department of Psychiatry, Yale University School of Medicine, 333 Cedar Street, New Haven, or 562-1161, Ext. 617. No registration fee; open to all physicians.

Seminars sponsored by the Connecticut Valley Hospital, held in Merritt Hall Auditorium

Visiting faculty—Connecticut Postgraduate Seminar

November 5 2:30 P.M.

"ECT and Other Physical Therapy Modalities," David J. Impastato, M.D.

November 8 10:30 A.M.

"The Psychotherapy of Obsessive States," Leon Salzman, M.D.

Contact: Iago Goldston, M.D., Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Inc., Fairfield Hills Hospital, Newtown; or Sal O. Prins, M.D., Director of Training, Connecticut Valley Hospital

No registration fee; open to all physicians.

SURGERY

October 9 1:30 P.M.

Congenital Ophthalmological Anomalies

Combined Clinical Meeting of Sections on Ophthalmology, Connecticut State Medical Society and Yale University School of Medicine

Speakers: Harold F. Falls, M.D., Professor of Ophthalmology, University of Michigan School of Medicine, and Rufus Howard, M.D., Assistant Professor of Ophthalmology, Yale University School of Medicine.

Program: 1:30 P.M., Eye Clinic, Yale-New Haven Medical Center; 4:30 P.M., Discussion, Brady Auditorium, Yale Medical School; 6:00 P.M., Social Hour, 7:00 P.M., Dinner, Governor Eaton Room, Park Plaza Hotel.

Contact: Dewey Katz, M.D., Hartford, 522-8398, or Dr. Howard, New Haven, 562-1121

No registration fee; open to all opthalmologists and members of the Eye Section

Special Article:

Behavioral Toxicity of Psychotropic Drugs:

III. Effects on Perceptual and Cognitive Functions
IV. Effects on Emotional (Mood) States

Alberto DiMascio, Ph.D., Donald R. Giller, A.B., and Richard I. Shader, M.D.

In a previous article[1], the following definition of "behavioral toxicity" was developed and explained:

> "Behavioral toxicity" is a phrase used to denote those pharmacological actions of a drug that, when administered with the dosage range in which it has been found to possess clinical utility, produce—through mechanisms not immediately specifiable—alterations in perceptual and cognitive functions, psychomotor performance, motivation, mood, interpersonal relationships, or intrapsychic processes of an individual to the degree that they interfere with or limit the capacity of the individual to function with his setting or constitute a hazard to his physical well-being.

In that article a review was made of psychotropic drug actions on psychomotor functions (including driving) as they fell within the scope of this definition. In the present article, the "behavioral toxic" effects of psychotropic drugs as they pertain to perceptual-cognitive functions and to emotional (mood) states will be summarized.

III. Perceptual-Cognitive Functions

Perceptual-cognitive functions are those aspects of human functioning involved in the subjective experiencing of a change or difference in objects or events in an individual's environment and include those mental processes essential to the processing, storage and incorporation of these changes into an organized system used in guiding one's behavior.

Researchers in the area have employed a variety of tests tapping attributes of perceptual functioning[2 3] such as time or size estimation and sensory input organization. Generally, these researchers have reported that whenever antipsychotic drugs (chlorpromazine) and antianxiety drugs (meprobamate and chlordiazepoxide) alter perceptual processes they act to slow them down slightly and to dull their sensitivity (i.e., thresholds). These drug-induced alterations in perceptual phenomena have included impairment of such diverse processes as size estimation[4], auditory discrimination[5], detection of apparent motion[6], concentration and focus of attention,[7-10] and rate of stimuli influx per unit time.[11-15]

These alterations in perceptual processes would seem to constitute "prima facie" evidence for adverse behavioral drug effects. As with laboratory tests of psychomotor performance, however, these laboratory tests also have little predictive value for more complex non-laboratory situations. Impairment of gross behaviors, that have as their bases one or more of these functions, have not been reported in psychiatric patients undergoing pharmacotherapy.

With regard to those mental functions that are essential to the processing, storage and incorporation of information to be used in guiding behavior, considerable evidence exists in humans indicative of drug-induced decreased efficiency. *Memory* (immediate recall) was impaired in both normals and in schozophrenic, psychoneurotic and depressed patients undergoing drug therapy with diazepam, meprobamate, chlorpromazine, nialamide, and isocarboxazid[16-20]. *Reasoning* ability (organizational and problem solving abilities)[21 22], and capacity to abstract (judgement and learning of conceptual relationships)[22-28] declined after meprobamate,

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chlordiazepoxide and chlorpromazine. The *mental speed* with which a simple task (arithmetic ability) was carried out was slowed by meprobamate, diazepam or chlorpromazine[8 29 30-32]. *Learning* (incorporation of new information or new relationships) was deleteriously affected in normals and in patients undergoing drug therapy: meprobamate, diazepam, trifluoperazine, chlorpromazine each have been shown to retard the learning process[16 17 29 32-37]. The processes described above should not be considered as isolated independent functions, but as parts of complex patterns of behavior that are highly interrelated with, and dependent on, the flow of internal and environmental events. Vestre[34], noted that when learning was carried out under chlorpromazine, retention of the material was not as great as when done under the placebo. In extrapolating from this finding to learning (or relearning) accomplished in psychotherapy, he questioned the efficacy of concomitant pharmacotherapy. A similar "adverse" effect of drugs on psychotherapy has been widely proclaimed by many psychoanalytically oriented therapists—without, however, experimental substantiation of their claims. Ostow[38], for example, suggested that pschotropic drugs decreased the amount of libido available to the ego and thus made psychotherapy difficult. Savage and Day[39], reported that reserpine caused patients to avoid painful issues and thus retarded psychotherapy. Sufficient subsequent controlled studies exist countering these claims.

A note of caution must be made here. *The reader is advised that such effects as have been described (or will be presented in later sections) are not an essential accompaniment to drug administrations. The articles referred to in the above sections have been selected from among a multitude of others because they document the adverse effects of psychotropic drugs that may occur.* In most instances, the authors of these articles clearly point out that these effects occur only in some patients, in individuals with specific personality characteristics[2 30-33 35-40], only at specific dosages, or only at certain times during the course of extended drug usage.

In addition, the fact that meprobamate, chlordiazepoxide, chlorpromazine, and imipramine are the most often cited drugs, does not mean that the various effects occur only after these drugs: their repeated citation merely reflects the fact that they have been more extensively and detailedly assessed.

IV. Emotional (Mood) States

One of the major useful pharmacological properties of psychotropic agents is the capacity to alter emotional or mood states in certain "clinically desirable" directions; i.e., to reduce anxiety and fear, diminish hostile-aggressive expressions, relieve depressive-guilt feelings, or attenuate euphoriant manic affect. Some agents may also alter mood in a manner or direction that may be considered "adverse". There are two major types of such drug-induced mood changes that have been reported: "paradoxical" and what we shall call "pendular" effects.

"Paradoxical" drug effects are those alterations in mood in a direction opposite to the "clinically desirable" one for which the drug has been prescribed. Increased anxiety has been reported with meprobamate[41-44], the benzodiazepines[45-47], the phenothiazines[48-53], MAO inhibitors[54-56], and imipramine[57 58]. Deepening of depressive affect by antidepressants have also been noted[58 59]. This phenomenon has been reported, however, only in individuals without pathological levels of depressive affect. Increased hostility has been reported after chlorpromazine[60-63], tybamate[64], and particularly after the benzodiazepines[46 56 65-73].

"Paradoxical rage" is a phenomenon reported to be induced by chlordiazepoxide[66 67 70], and diazepam[74]. Feldman[74], described the occurrence of this behavior as follows:

> ". . . many of the patients receiving (diazepam) displayed a progressive development of dislikes or hates. The patients themselves deliberately used the term "hate". This hatefulness first involved non-significant figures in the patients' environment, progressed from there to the involvement of key figures such as aides, nurses and physicians, and went on to the involvement of important figures such as parents and spouses. The phenomenon was progressive and in some instances, culminated in overt acts of violence . . ."

Indeed, even acts of violence such as murder and suicide have been attributed to the rage reactions induced by chlordiazepoxide and diazepam[75-78].

While most clinicians and investigators have claimed this phenomenon to be "paradoxical" (i.e., unexpected and unpredictable), several recent reports[72 73 78 79], have shown the release of hostile-aggressive feelings to be a not infrequent consequence of some benzodiazepines. These authors suggest a number of reasons why the phenomenon is not more universally known and recognized: the amount of drug-released hostility often is not marked; the comparative insensitivity of clinical observation versus the sensitivity of the hostility scales utilized in their studies; and the fact that for many patients the release of aggressiveness may be therapeutically beneficial—when channeled appropriately—and thus may be considered part of overall therapeutic movement rather than as drug-induced behavior. These authors further hypothesize that it may be only in those patients with a history of poor impulse control or aggressive, destructive behavior that chlordiazepoxide can release sufficient hostility to result in "rage reactions"[72]. Thus, "rage reactions" should not be considered as "paradoxical" actions of the drug but, in such individuals, a "predictable" effect.

Various explanations have been formulated to explain the paradoxical anxiety and hostility noted after chlorpromazine; Freyhan[81], and Goldman[82], postulated these to be directly determined pharmacologic drug actions, while Sarwer-Foner[83], Azima and Sarwer-Foner[84], Klerman, *et al*[85], and Heninger and DiMascio[52], have postulated that these effects are secondary responses of a drug-personality interaction centering about the meaning of the psychomotor inhibiting and sedative-hypnotic effects of the drugs.

DiMascio and collaborators[45 46 58], as well as McDonald[73], have offered the experimental finding that increased anxiety with benzodiazepine derivatives—and increased depressive affect after imipramine—occurs only in those individuals who do not initially manifest a marked degree of anxiety or depression. They suggest that clinical reports of such a nature may be due to the administration of the drugs to inappropriately selected patients.

"Pendular" drug effects are those drug-induced alterations that proceed in a "desired" direction to the degree that the resultant state tends towards the opposite state for which the drug was initially administered. For example, chlorpromazine is known to reduce the affective expression of excited manic patients to a level that depressive affect may become the prominent feature[86]; the MAO inhibitors and imipramine relieve depression—substituting for it, in some instances, a state of euphoria[60 63 86-90]. In addition, numerous physicians have expressed concern about the excessive relief of anxiety below a "good" and "necessary" level. These "pendular" changes often may progress to the degree that they require cessation of the medication and active treatment by other medications.

In summary, it has been pointed out that psychotropic drugs are of great value in altering human behavior and emotions that have become disturbed. These drugs, however, also have the potential to release or produce changes such that a patient will show a disruption of, or disturbance in, his behavior and emotions in areas where none had been present, or have an exacerbation of his present symptoms. In either case, unless the treating physician is aware that the treatment he has instituted may be the cause of these changes, he can make the assumption that the patient's condition is deteriorating and react by increasing the medication. An unpleasant and potentially detrimental spiral of drugs—disturbed behavior—more drugs—more disturbances, etc., may be created.

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Electrocardiograms of the Month

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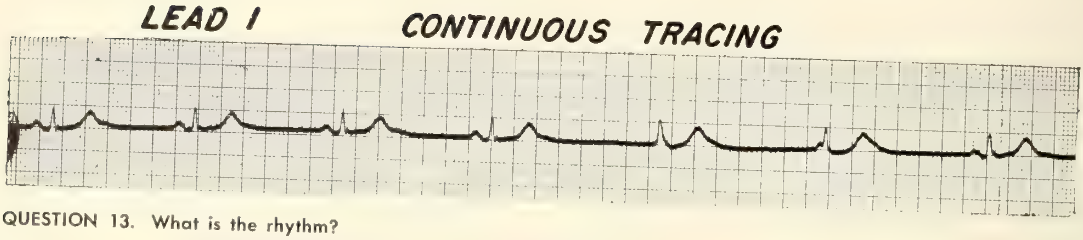
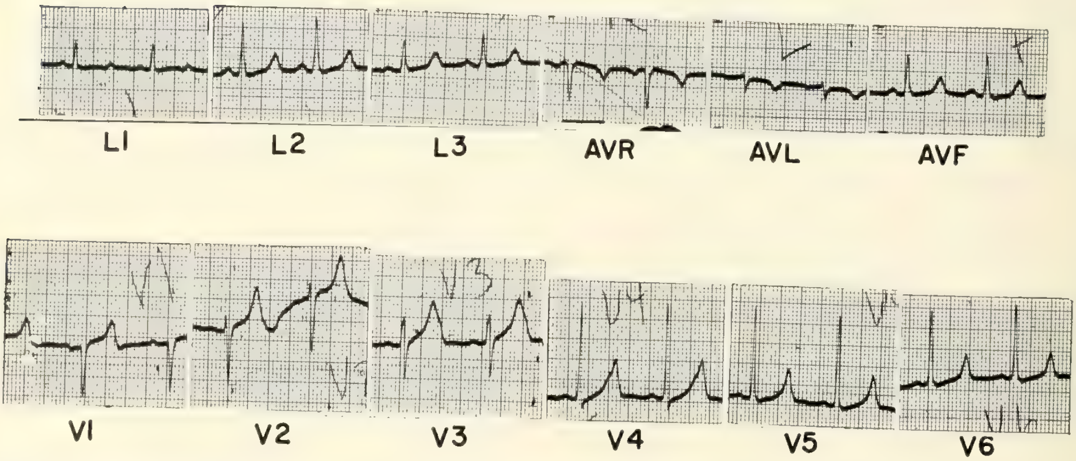


QUESTION 13. What is the rhythm?



QUESTION 14. This tracing was obtained from a fifty-year-old woman with uremia. What electrolyte abnormalities are suggested by the electrocardiogram?

Electro-
cardiograms
of Month

ELUCIDATION

QUESTION 13. The first four beats are regular sinus beats. The fifth beat is delayed and is not preceded by a P wave; the QRS appears widened. This beat is a "nodal" escape beat. The QRS deformity is caused by a retrograde P wave. The next beat is also a nodal escape beat with a sinus P wave superimposed on the initial portion of the QRS. The P-R interval is too short for this P wave to be conducted. No retrograde P wave is present because the atrium has been depolarized by the sinus beat. The last complex is again regular sinus rhythm.

Escape beats occur when there is suppression of the dominant pacemaker of the heart and a lower center takes over the pacemaking function. In this instance, the sinus node is the dominant pacemaker. When it slows markedly or arrests, after the fourth beat, the "node" (actualy A-V junctional tissue or bundle of His) becomes the pacemaker for the fifth and sixth beats. The sinus node then resumes the pacemaking function as the rhythm returns to regular sinus. The usual cause of sinus arrest is increased vagal activity, but drugs (such as digitalis) or heart disease (disease of the coronary artery supplying the sino-atrial node) may also lead to sinus arrest.

QUESTION 14. The rhythm is regular sinus rhythm at a rate of 75. The T waves are sharply peaked as best demonstrated in V_5 and V_6. The QT is prolonged to 0.46 second, due primarily to a long, straight S-T segment best seen in lead I and aVl. The narrow, peaked T waves are found in hyperkalemia. The prolonged isoelectric S-T segment is a result of hypocalcemia. This patient had a serum calcium of 7.5 mg. per 100 cc. and a serum potassium of 6.8 mg. per 100 cc. These electrolyte abnormalities are frequently found in severe renal insufficiency and are often reflected in the electrocardiogram.

Incinerators and air pollution

Installers of any new incinerator in New York State after January 1, 1968, must prove by actual test results that it meets State air pollution control standards, it was recently announced by the State Air Pollution Control Board.

Incinerators that do not meet standards will not be allowed to operate until remedial action is taken.

The new requirements were enacted by the State's Air Pollution Control Board to control incineration of solid wastes, a major source of air pollution in the State. An estimated 34 billion pounds of solid wastes are disposed of by incineration.

A permit for any installation after January 1 must be obtained from the State Health Department's division of air resources. Test specification of incinerators on sale in the State will be on file with the Department, and permit applicants will be responsible for determining the acceptability of a proposed installation.

Incinerators built prior to January 1, 1968, also come under control with the new regulations and will be required to meet standards that vary according to their construction date.

Reprinted from New York State Journal of Medicine, February 1, 1968.

Connecticut Medicine

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Connecticut State
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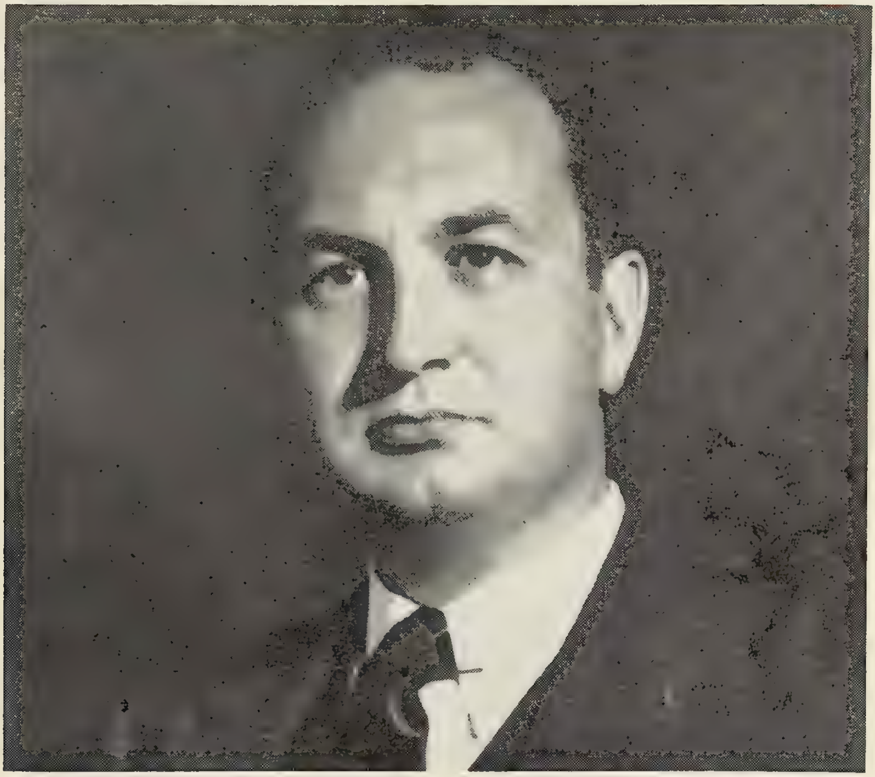
Volume 32/November 1968/Number 11

CARDIOVASCULAR SURGERY ISSUE: H. C. Stansel, Jr., M.D., *Guest Editor*



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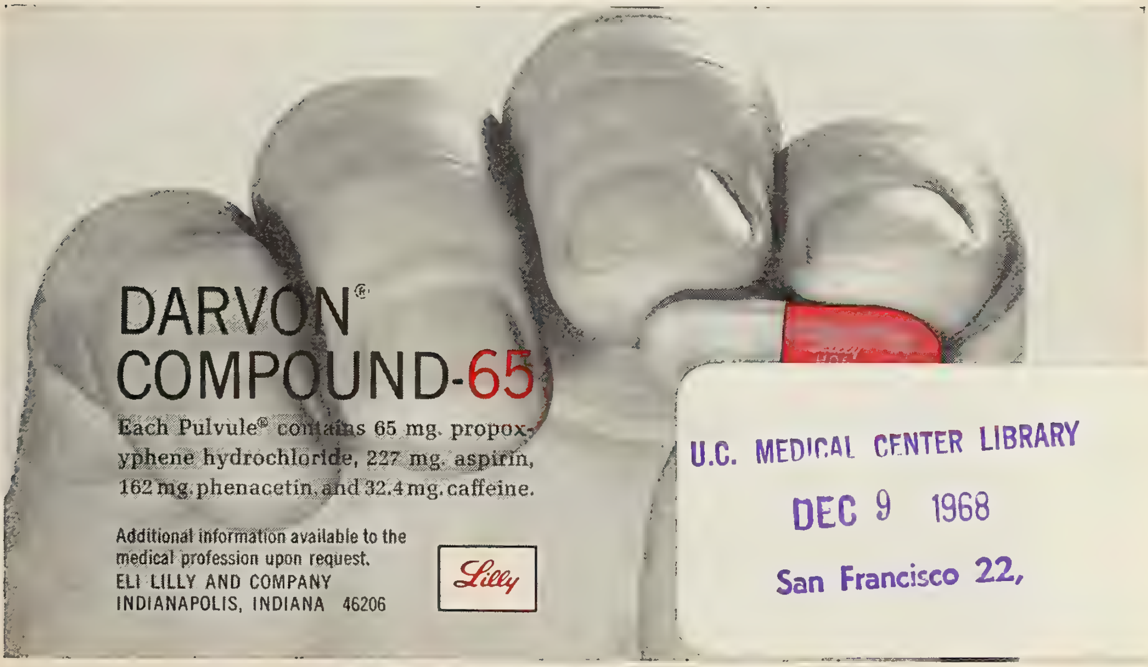

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Connecticut Medicine

editorials

A Definition Of Death: Ethical And Legal Questions Posed By Recent Advances In Medicine

One reason why giving a new heart for an old one attracted so much attention of the world is because someone must die to make another live. This is aside from the fact that surgeons doubtless are moving very far and very fast in their zeal for knowledge and at times for fame. The public is worried whether some over enthusiastic surgeon will declare the donor dead before death has occurred in order to have a viable heart to transplant. The public is also worried that the demand for hearts will outstrip the supply and how will the priorities for eligibility as a recipient be established. Who will make such decisions? Will they be in conformance with medical ethics and law?

Since death is inevitable for the donor of a heart or liver, it is essential that we understand how to identify death and when it occurs rather precisely. Legally and from a religious point of view there is such a moment. It is the irreversible cessation of heart action or respiration or both, although biologically death might extend much longer. However, heart stoppage and cessation is not enough because the heart can be restarted after it has ceased beating, similarly with respiration. If the heart and respiration can be kept going then perhaps the death of the brain should be the legal sign of death, as determined by the electroencephalogram (EEG) dilated unresponsive pupils and absent reflexes.

These questions are being discussed throughout the entire world. The criteria for determining death that have received acceptance by many physicians in most countries are those that determine the death of the brain such as flat EEG, no respiratory movements for five minutes after cessation of mechanical respiration and absent reflexes including the pupils. If these are present the patient should be considered dead. Of equal importance, however, is that the determination that these criteria have been met should be made by the medical team which is in charge of the dying donor and never by the medical team responsible for the recipient patient.

If this is done it will minimize the impact upon medical practice of such questions as, should we attempt resuscitation on all people with cardiac and respiratory arrest. Should we consider the duration of the heart stoppage to avoid producing a living body without a thinking brain? We all dread responsibility for producing a "vegetable" existence for the patient. The fact is, as Appel[1] points out, that physicians have been successfully sued for failing to attempt to restore a heart and as well for doing just this. There are situations where even the criteria of death mentioned above have their exceptions. It should be kept in mind that after barbiturates or prolonged exposure to cold there may be no activity in the EEG for sev-

ABOUT THE COVER

The recent developments in cardiovascular surgery described in this edition of *Connecticut Medicine* are the results of intense dedication by many investigators in the field. If any one individual is primarily responsible for the stimulus which has opened up this exciting new era, it has been Dr. Robert Gross. It was his initial report in 1939 of the successful ligation of the patent ductus arteriosus that really provided the spark. The tremendous strides made in cardiology by those closely associated with him and others also had its greatest impetus from his pioneering work. Not only is he known for his superb clinical investigation, but perhaps better as a teacher with many outstanding former pupils scattered over the world. It is, therefore, with pride that we dedicate this edition of the *Journal* to Dr. Robert E. Gross.

H. C. Stansel, Jr., M.D., *Guest Editor* eral hours yet full recovery is the rule. After being struck by lightning all metabolism including that of the brain stops for relatively long periods, yet full recovery can and does occur.

When organs are available, then who has a right to give permission for their removal. Legislation has been enacted in some states specifically permitting the willing of the cornea to eye banks and to science. If one can will a part why then can't one will other organs. In thirty-one states some type of legislation permits this but with great variety. Specific permission in writing by the donor obviates delay, unless it is difficult to secure this evidence that a proper will has been made and this takes time when organs are needed immediately after a fatal accident. This delay may be even worse if the accident is far away from the home of the deceased.

Consent for a transplant procedure must also be obtained from the recipient of the organ and it is stated that such consent must be "informed." Can the recipient be expected to completely understand the procedure proposed, its potential benefits and its possible adverse effects. He must be made to understand fully the present condition as it exists without transplantation and what he might expect if he receives no transplant. Also he must know that if the heart transplant for example fails he will die promptly. He needs to know that it can be only partially successful, in which case he might live but his life might be worse than it has been because of present insufficient knowledge and ability to overcome the rejection process and the restoration of the lymphatic return. It is recognized that the patient is in an inadequate frame of mind not to trust his physician's advice. Even if the closest relatives are brought into the decision making process their ability to help the patient come to a decision is just as much handicapped by lack of understanding and by personal emotions. The physician in charge of the recipient patient must himself be in a position of certainty in advising the patient that no other procedure or treatment is available to prevent his imminent death. Furthermore, we may never have enough donor organs available to meet the demand which will grow as transplant techniques improve. For then strict medical indications for organ transplantation will be lessened, so that more and more recipients will become eligible. Who will then decide which patient should receive the organ and which not?

What guidelines we have to protect the patient and the physician were developed during the Nuremberg trials following World War II when the whole world was appalled to find the irresponsible human experimentation practiced by the Hitlerite physicians mostly upon Jews before they were burned in the gas ovens. Based on the principles used during these trials the World Medical Association adopted the Helsinki Agreement which has been adopted by most Nation members of the U.N. and most medical national societies.

As worked out in hemodialysis units where the number of needy patients greatly exceeds the supply of kidneys, the general idea is to develop legal, ethical and moral guidelines to exercise some kind of control on this type of research and on those scientists who conduct it. Among these guidelines should be one that the physician should resort to an old and proven safeguard included in the Principles of Ethics of the American Medical Association that involves the readiness to use consultants. This principle would serve a valuable purpose in bringing available knowledge, interests and approaches to a very serious problem. Other disciplines such as law, sociology and religion should also be involved. People will need to be educated that the practices and research contributes to scientific advancement at the same time protecting the rights and dignity of man and sanctity of life.

Of course organ transplants will continue. Especially heart transplants, however, should for the present be considered not as an accepted form of treatment but as a form of research[2]. Therefore, only teams of physicians and medical scientists with demonstrated ability in the procedure gained from research and who have established a reputation for responsibility in the ethics of human experimentation should be permitted to carry out such research.

There is no sidestepping the fact that procedures which cannot be called anything but experimental have through the ages been done on human beings. But at present we are in need of guidelines. Beecher's statement in the *New England Journal of Medicine* sums them up well. In substance they are "that the subject of an experiment involving any risk must stand to benefit from it. That his informed consent must be obtained to the fullest degree possible and more important than any specific rules, that have been devised, the investigator must be intelligent, informed, conscientious, compassionate, responsible."[3]

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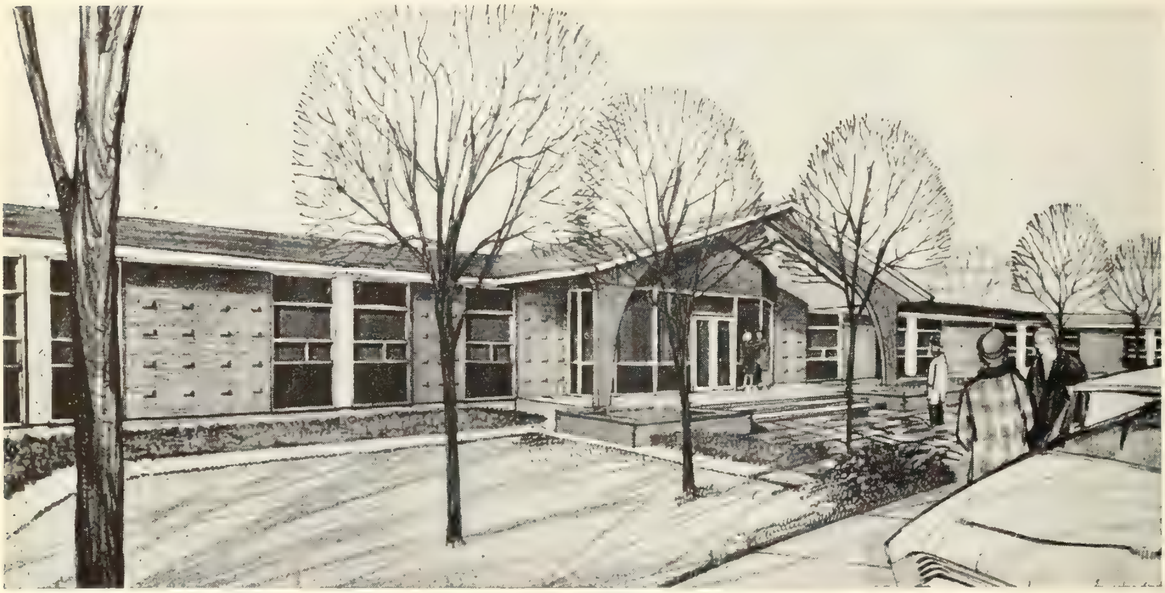

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when this is not an issue that then we must devote ourselves to work in the best interest of humanity.

L.H.N.

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The Declaration Of Helsinki

The Declaration of Helsinki contains recommendations for the guidelines of doctors in clinical research and was adopted by the World Medical Association in 1964. Its basic principles are as follows:

1. Clinical research must conform to the moral scientific principles that justify medical research and should be based on laboratory and animal experiments and other scientifically established facts.
2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.
3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefit to the subject or to others.
5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.
6. Non-therapeutic research on human beings must never be undertaken without their informed consent, but that regardless of consent, responsibility for the procedure always remains with the medical investigator.
7. In research combined with professional care use of the therapeutic measure under investigation is justified in the acquisition of new knowledge only if it promises therapeutic value for the patient.

Science Tools: 30.
The Prosthetic Heart Valve

There has been a gradual improvement in operative mortality in valve replacement surgery by the introduction of atrial pacing to control arrhythmias and also to augment cardiac output in the immediate post-operative period. The late survival of patients with implanted heart valve prostheses is still not much better than 50 per cent after two years. Thus the first two years are the critical period after which the outlook for continued survival improves. Dr. Starr, who began implanting the Starr Edwards prothesis in 1960 reported upon 650 patients at the Second National Conference on Prosthetic Valves and emphasized the remarkable decline in the early or post-operative mortality. The causes of the late mortality have been pinpointed and one by one they are being brought under control.

Dr. Duvoisin from the Mayo Clinic reported that of 1355 patients with implanted valves between 1960 and January 1968, 52 per cent were alive and with a good result after five years. The problems that came to be recognized were thromboembolism, perivalvular leaks, infection, and in the older models ball variance. In addition to overcoming these problems there was recognized the need for a valve which does not interpose resistance to central flow and which also creates less turbulence than other presently available valves. The need to reduce thromboembolism, and to produce a valve which more nearly functions like a natural valve were extensively covered at the conference.

A most promising innovation in valve design has been cloth encapsulation of the valve seat to reduce embolization The high incidence of thromboembolism associated with the artifical prosthesis despite the extensive use of anticoagulants has in fact been the principle argument advanced in favor of using valve homografts. It is the blood metal interface which is primarily responsible for the high incidence of thrombi formation. The use of a cloth cover on the valve seat is intended to facilitate tissue growth and a tissue blood interface it was hoped would reduce the incidence of thrombus formation.

With the older model Starr Edwards ball and cage mitral valve the metal of the valve seat and cage were exposed to the blood flowing through the valve and the incidence of embolic complications had been as high as 61 per cent. Since 1965 when a cloth covered seat was introduced the thromboembolic complications had dropped to 7 per cent. A similar change in the aortic valve led to a decline in thromboembolism from 29 to 9 per cent. When the cloth cover was extended to the struts of the cage in March of 1967, it reduced the

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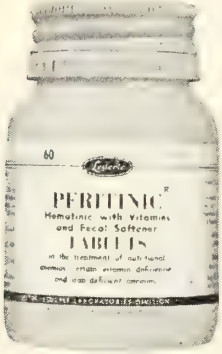

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noise of the valve operation, but also greatly reduced thromboembolism to one in forty-five patients. Cloth cover of the valve seat has also helped reduce the incidence of thromboembolism with several new mitral disc valves. The most recent model of the Starr-Edwards prosthesis features a hollow metal (stellite) ball in a teflon encapsulated cage to overcome the problem of ball variance i.e. deteriorative change that developed with the silicone rubber balls used in the earlier models.

Several disc type valves were developed primarily to avoid interference with the left ventricular outflow tract which was observed in some patients with ball and cage valves. Disc type valves of various types were reported upon at the conference. Dr. Arthur C. Beall, Jr. reported on results obtained with a dacron covered disc prostheses developed at Baylor and said only three instances of thromboembolism have occurred among 202 patients receiving the valve. This dramatic reduction in the incidence of thromboembolic complications with a cloth covered disc prosthesis has led to a cautious elimination of anticoagulants by some investigators, especially since chronic anticoagulation causes its own complications.

The occurence of perivalvular leaks, though rare (2 of 178 patients required reoperation), has led to fashioning of a prosthesis fitted with metal prongs which anchor the valve to the mitral or aortic orifice. This Magovern valve largely eliminates the time spent in suturing conventional valves in place and also offers the advantage of decreased perfusion time during surgery. The ideal valve of course would be one that eliminates central occluders and two novel valve designs which approach this theoretical ideal were reported at this conference.

One model was described by Randolph M. Ferlic of the Minnesota Medical School. It is shaped like an inner tube and the poppet is made of titanium. When closed it sits upon a central post connected to the valve ring by a single strut. It combines the low profile of the disc valve with the low obstructive characteristics of the ball valve. Another new model is a hingeless valve designed by Juro Wada of Japan. It consists of a single leaflet which pivots 75 degrees upon opening to present a minimal obstructive surface to the flow of blood through the valve. It has been implanted in thirty patients of whom three died but the remaining twenty-seven have had no thromboembolism and have not been on anticoagulants. The flow characteristics of the Wada hingless valve with single leaflet show much less resistance to central flow and less turbulence than other presently available valves.

One new valve, the trileaflet valve developed by Dr. Charles A. Hufnagel of George Washington University is fashioned from flexible synthetic cloth. It was not reported at the conference, but it has already been implanted in seventy-five patients during the past year and is attracting considerable interest among thoracic surgeons.

Obviously our present valves represent compromises which are imposed on us by factors which we must accept. There have been excellent results and there will be better ones yet. It is sobering, however, that as many as half of the patients who have had heart valves implanted are not here anymore.

L.H.N.

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Thromboembolic Complications In Patients With Starr-Edwards Valve Prothesis

Over 20,000 Starr-Edwards[1] valves have been placed in human hearts since the first successful ball-valve prosthesis was achieved in 1960. Over the years the operative mortality and morbidity of the insertion of this type of artificial valve in aortic and mitral positions have been reduced to a now acceptable level. One serious complication of prosthetic valve replacement, systemic thromboembolism still remains. In Akbarian's series[2] of insertion of such valves in 283 patients thromboembolism developed in 68 patients (24 per cent). As might be expected it occurred more frequently in those not receiving anticoagulant therapy—29 of 52 but only in 24 of 124 treated patients. In four patients abrupt discontinuance of anticoagulant therapy led to fatal thromboembolism. In two it was stopped because of gastrointestinal bleeding, in one in preparation for tooth extraction and one patient discontinued anticoagulants on his own.

The most common vessels involved with thromboembolism were cerebral (57), coronary (8), renal (2), splenic (2), retinal (1). In two patients the clots were on the prosthesis and the ball became immobile. As a result of the embolic episode 17 of 68 patients died. The usual complications of anticoagulant therapy—bleeding occurred in 23 patients. We do not know in how many inadequate therapy occurred but clearly anticoagulant therapy must be carefully and successfully carried out if thromboembolism is to be minimized.

Akbarian's series revealed as others have that late embolic problems following prosthetic valve replacement have been an important cause of disappointing results. The reports varied only as regards the site of the prosthesis—mitral or aortic, the use of anticoagulants, the cardiac rhythm, and duration of follow-up. The 24 per cent incidence of thromboembolism in Akbarian's series is probably low since he accepted as "embolic episodes" only those that could be diagnosed with certainty. Some of lesser severity must therefore not have entered into the statistic.

Previously reported practices with respect to anticoagulant therapy following prosthetic valve insertion have differed widely from center to center. Some groups do not give anticoagulant therapy at all[3]. Some give it to selected patients[4] while others use them routinely and indefinitely unless there is an important contraindication. This appears to be justified because obviously anticoagulant therapy was definitely beneficial especially to the patients with aortic valve prothesis. In mitral valve prosthesis, anticoagulant therapy appeared less protective against thromboembolism.

An additional proof of the value of anticoagulant treatment comes from an analysis of aortic valve prosthetic cases. Previously untreated patients following their first embolic episode showed a significant reduction in the incidence of further embolism once anticoagulant therapy was instituted. One element of doubt, however, is derived from two observations. In one the adequacy of control therapy seemed to bear no significant relation to freedom from embolic complications in any of the patient groups studied. Another is that the overall incidence of embolism following prosthetic valve insertion tends to increase with the duration of follow-up There thus appear to be a leveling off after two years of follow-up in Akbarian's and other series too[5].

The disputed efficiency of anticoagulant therapy in preventing thromboembolic complications has stimulated sustained interest in improving the prosthetic design. Preliminary follow-up of patients with the newer model Starr-Edwards prosthesis (1200 aortic valve and 6120 mitral valve) suggest that embolism may be much less of a problem[1]. We are still unsure of the role of cardiac rhythm itself in the thromboembolic complication[6].

Akbarian's study is timely because it can serve as a basis for comparison with valve prosthesis of improved design in the future. In the meanwhile it behooves every physician who is to control anticoagulation in patients with valve prosthesis to sharpen his skill in maintaining anticoagulation therapy successfully and avoid the 8 per cent serious complications usually reported from the use of anticoagulant drugs.

L.H.N.

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Epidemiologic Aspects Of Vascular Disease Of The Brain

Because of increasing proportion of elderly people in the population there has been an increase in the incidence of central nervous system vascular deaths. Only coronary heart disease and malignant disease are greater killers than cerebrovascular disease. There is however a wide variation in its incidence around the world and in this country from one region to another. In Japan it is 208.6 per 100,000 population. In Australia, 118 per 100,000, in the United States, 100.4 and in Mexico, 35.5.

Yates British study of trends in cerebrovascular death rates showed that death due to hemorrhage declined while that due to thrombosis and embolism increased and this change was also found in these diseases seen at autopsy in three Manchester hospitals. This pattern corresponds with the parallel increase in deaths from ischemic heart disease over the same period. There appears also to be a seasonal swing in death rates from cerebrovascular disease with a summer low and a winter high. In Australia the incidence was 3.3 per 1,000 per year greatest between ages 70-79. At age 60 it was 2 per cent per year.

The prognosis is depressing. About one in three dies during the first attack[1]. Of the survivors one in three will have a recurrence in the next two years and what is worse recurrences are most common soon after an attack. Half of such recurrences occur within the first six months. In recurrent attacks the mortality rate per attack remains about one in three among affected people. But there is a small proportion who suffer multiple small attacks that are not fatal. Unfortunately those who suffer at least one recurrent attack are much more likely to have further recurrences and two out of three of these will have recurrences within two years. This almost suggests that there is such an entity as "active cerebral vascular disease." Interestingly many cases perhaps the majority will have been in poor general health before their stroke while one-third will have definite premonitory signs of some sort and of these half have a stuttering type of onset.

Cerebrovascular disease is a generic name for a number of different entities. The great bulk of cases are due to cerebral infarction, 63 per cent in the Farmingham[2] study and 64 per cent in Wallace's. Cerebral hemorrhage is much less common when diagnosed by strict criteria or by autopsy. For example Wallace found 16 per cent, but only 4 per cent were found in Framingham. Subarachnoid hemorrhage and cerebral embolism are of approximately equal incidence and cause between 18—9 per cent of all cases.

It is interesting to compare this disease with other main categories of arterial disease such as coronary heart disease and peripheral vascular disease. In Framingham there was a much higher concurrence of two or more of these categories of disease than might have occurred by chance and of course this supports the well known concept of a common underlying cause for all these conditions. Wallace's study revealed that many cases arose as the result of an embolus following myocardial infarction. This might support the use of anticoagulants in this type of heart disease especially since a cerebral embolus can be such a devastating accident complicating an otherwise successful recovery from myocardial infarction.

Because of the different possible causes of stroke it is imperative that such cases receive full attention and investigation. Not to do this may lead to a failure to recognize a potentially remediable condition since as noted above a small proportion of apparent strokes are due to causes such as cerebral tumor, subdural hematoma and also we must search for an antecedent cardiac condition which must always be considered.

Unhappily the prospect of long term survival following a cerebrovascular attack is not good. More than half of the cases having an initial stroke will be dead within two years while among those with recurrent attacks over two-thirds will be dead within this period. Surprisingly the incidence of severe physical and mental impairment is not too great. The majority attain some independence in daily living. But a minority do continue to need help of some sort but are able to live at home. Little more than 10 per cent require as much as three months in a hospital or nursing home and only a very small fraction seem to require continued nursing care.

Since we find these cases occurring late in development of atherosclerosis it is understandable why our therapies are inadequate and why we need to work out in greatest detail the natural history of this disease so as not to fall victim to our belief in any brilliantly successful method of therapy.

L.H.N.

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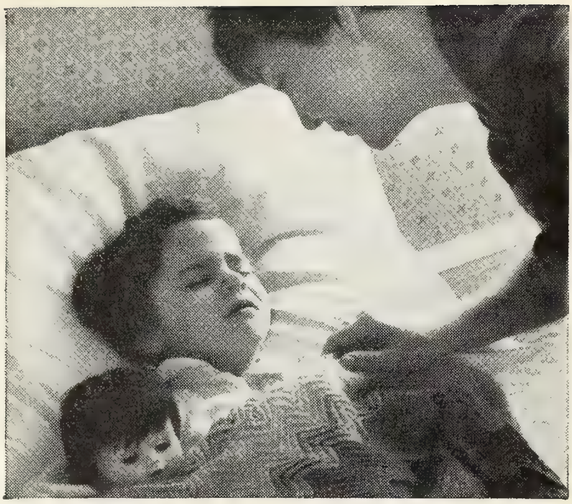
To Prevent Heart Disease And Death From Myocardial Infarction

Morris[1] has collected figures on a population of 7,000 male British physicians aged forty to sixty-four in whom sudden death appears to be more than twice as frequent as other types of death ascribed to ischemic heart disease. If this is true what is the place of myocardial infarction? In this country the best source of information is out of Framingham[2] in which one out of six men who developed symptoms of new heart disease during a twelve year observation period died unexpectedly within less than one hour. These deaths appeared to have made up 40 per cent of all male coronary deaths during the period of observation. This points up a whole gamut in the biology of myocardial infarction. Some patients present the classic clinical picture of myocardial infarction. Others sucumb in a few minutes to fatal arrhythmia. Some develop angina pectoris, while others go on to progressive heart failure indistinguishable from myocardial weakness from other causes.

Two parallel trends can be discerned in our struggle to prevent heart disease and deaths from



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Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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this source. One is evidenced by the 50 million venture contemplated to study the usefulness of preventive dieting. The other is away from preventive aspects of coronary heart disease (CHD) that has been so favored for a decade or so, toward the coronary care unit (CCU) and the philosophy of immediate action. This as Biörck[3] points out seems to be a shift from strategy to tactics. Our aims then appear to be twofold. One is to postpone the first manifestation of CHD (especially myocardial infarction and lethal arrhythmias) and to postpone repeated attacks. The other is to reduce the acute mortality and then improve the condition of the survivor.

The strategic approach derives from a biological philosophy based on animal experimentation and epidemiological surveys. It tries to modify and counteract pathogenetic mechanisms particularly in persons earmarked as especially vulnerable candidates for future disease. The tactical approach on the other hand is an expression of a humanitarian philosophy; to fight death and save life vigorously, unyieldingly and at any price. Although these goals are not mutually exclusive in this country, we must be aware that for years to come in many countries perhaps even in this country while so much wealth is pouring into the Vietnam war to the detriment of education and social welfare medical manpower will remain scarce and the cost of acute medicine will be mounting. What then may be the prospects of each?

We have learned a lot about vascular pathology from studies of biochemistry in rabbits. Disease as a patterned response may also be studied in human populations where nature or history create their own experimental conditions, for the agent of disease may be neither outside nor exclusively within. Disease may develop as a result of maladaptation of an old-fashioned biological machinery exposed to the forces of quite another life situation than it was evolved to master. In our zoological ancestors atherosclerosis of the aorta with advancing age seems to be as frequent in many species as in man. It is observed for example in some wild pigeons which may die of myocardial infarction and there may even be epidemics of this disease in some birds during the breeding season.

The human pattern of coronary artery disease is found in the large primates as gorillas and chimpanzees in whom the disease is observed even before puberty. In zoological gardens effects of physiological and psychological responses to "social" stimuli of various kinds upon the heart vasculature appear as well as the influence of age per se. In fact the influence of emotional factors upon the circulation have been shown to operate upon primates exactly as they do within ourselves. Among which are sexual frustrations and restrained aggression. Such studies may provide the missing link in our search for causes and mechanisms of human disease. Perhaps we share with these animals enough of our emotional behavior or even conceptual frame of reference to permit an experimental analysis of the ways of life that lead to disease and death.

Human physiology and pathophysiology must be conceived in terms of our genetic environmental past. The genetic element has been emphasized by Dr. Paul Dudley White[4] and studies on family trees and on twins support this conviction. But there is always the interplay between genetic endowment and environmental damage. Accordingly the strategy of prevention before overt disease or after an infarction is based on the concept of diverting an inherently unfavorable course to a more favorable one. Studies of the preventive effects of reduction of blood lipids either by dieting or the use of drugs and the preventive effects of long-term use of anticoagulants and female sex hormones and of giving up smoking are underway everywhere. Those endeavors as well as those directed toward diabetic tendencies in coronary patients all belong to the strategic forces.

The evidence in favor of definite effect of lowering blood lipids is getting stronger. Leren[5] found a significant reduction of new angina and of recurrent infarction in 400 males who survived myocardial infarction for five years and under age sixty while sudden death was more frequent in patients with angina pectoris and abnormal electrocardiogram or both were not affected. Giving up smoking has been shown to improve prognosis[6] and preliminary data concerning antidiabetic measures in infarct patients with disturbed glucose tolerance are certainly promising[7]. The effect of such interference with pathogenetic mechanisms may in principle be of several kinds. There may either be no effect or delay of infarction but little or no effect on longevity if the patient survives. Or there may be delayed infarction and correspondingly delayed death. Or there may be delayed infarction and also more than correspondingly delayed death.

This variability of response to any therapy explains why it still remains to be seen whether the results will be substantial or only of marginal value as appears increasingly to be true of long term use of anticoagulation. Goffman[8] has for example recently expressed the opinion that blood lipid levels are of little prognostic value in already manifest CHD in persons over fifty and that moderate reduction of blood lipids will have no influence on life expectancy beyond fifty-five. Apparently diet changes in order to have an effect have to begin early and be drastic. The lower the dividends become with age the more imperative will it be to establish the predictive value of biological indeces in young individual and to act selectively on young candidates. Although most preventive measures might be accomplished by natural remedies, it is probably more in line with our present technology to expect that artificial means will take the place of natural ones and the use of drugs will be considered more acceptable than the cultivation of new habits.

The tactical approach can be seen in the remarkable and rapid development of the intensive care unit culminating in the coronary care unit (CCU). Within a short time an almost revolutionary situation has been created. Nevertheless Oliver et al in Edenburgh[9] has recently warned against making too optimistic predictions of the results of such treatment in the front line of the infarct battle. High fatality rates still prevail. Short term gains must still be weighed against longer term ones. A recent report from a London hospital[10] stated that of 150 patients treated in a CCU, 21 died and 129 survived, 10 of whom had been resuscitated from otherwise fatal arrhythmias. These figures are said to represent a reduction of immediate mortality by 50 per cent. However, other estimates for example those of Grendahl from Oslo[3] are much lower. Furthermore we do not as yet know whether the immediate gain will be maintained or lost during the following years.

This should probably become evident soon in view of the fact that MI recur most frequently within the first year or two after the preceding infarct[2]. Such follow up studies will determine how many lives saved were relegated to health or invalidism and for how long. Once established, however, the CCU have probably come to stay regardless of whether they add length to human life without quality.

L.H.N.

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An Experimental Method For Medical Teaching: 1. The Student-Centered Group. A Method For Self Learning

The educative process is complex and dynamic and there is merit in certain of the students complaints and their striving for new modes of learning. One technique has been tried in Britain[1] where Boddy and Backett have reported on turning the student into a teacher. In this country a method of programmed instruction[2] based upon utilizing the principle of reinforcement has been slowly invading colleges and institutions of higher learning perhaps too slowly, especially since medical science is growing at breakneck speed and the traditional boundaries of various departments have almost vanished. What appears to be necessary is that a community give up any role as an "intellect filling station."[3] Instead they need to understand the tentative nature of a scientific conclusion, to think critically and independently and learn to draw their own conclusions on the basis of available data.

Students somehow do not appreciate the active nature of the learning process. They tend too easily to rely on habit and routine in the solution of medical problems. Many grow up with a definite resistance to teacher authoritarianism. It is necessary therefore to search for a method to replace this attitude with one of feelings of esteem between both teacher and student. There is need to encourage students to learn from each other and to assume responsibility for their own education. After all this type of learning habit must be achieved since they will perforce have to remain students for life permanently after graduation.

Coppola and Gonnella[4] found that most of their students failed to consider how they would personally handle the problem of keeping up with expanding medical literature. They tended to view medicine as a well-defined and static body of knowledge from which the faculty is supposed to choose and convey to them the most pertinent part. Teachers were regarded as good or bad according to their willingness to assume an active role in conveying this crucial information. Those teachers who "passed out pearls" were regarded as helpful while those who required a student to work out his own conclusions were thought to be difficult, unwilling to 'teach" and hard to learn from.

Conflicting views of diagnosis and treatment or pathophysiology seemed to be undesirable impediments to learning because they made the students feel confused and uncertain. Argument from "clinical experience" had great weight for most of their students who often missed the point that experience can be distorted, misinterpreted or even poorly understood. The prevailing view was that the students were there to "learn something" and the teachers role was to teach "it" to them.

Active participation by students on rounds or in conferences was feared lest it open them to criticism or ridicule by some teachers. Thus a deficiency of understanding was regarded not as an opportunity for learning but as a mark of failure. Many students thus began to believe that to survive required that they stay in the background by not asking questions or participating in discussion. Thus they thought to achieve a degree of "safe anonymity." The views of students uncovered by Coppola and Gonnella stand in contrast to that of most educational psychologists who all recognize that learning requires active participation by the learner.

The students seemed ready to accept and use phrases like "routine blood work" or routine workup as substitutes for thinking and planning, an unhappy habit of many internes, residents and practicing physicians as well. The students also felt that many of the faculty held them in low esteem and this encouraged the very destructive habit of regarding each other as competitors for faculty approval in the form of better grades. These feelings were very strong so that not uncommonly a student would deny another access to lecture notes or other informational material.

From what was uncovered among feelings and attitudes of the student body, it was clear to Coppola and Gonnella that what was required was a radical change in the learners behavior. Content objectives which receive much emphasis in traditional teaching methods, should of course not suffer. On the other hand, the student who wanted to learn was invited to join a student-centered group. There is much evidence in the literature to support this stand on self-learning. Since the attitudinal and behavioral objectives were not being met by the traditional in this case surgical clerkship, the student centered group was instituted. The idea was to see whether beneficial results in the areas of critical thinking and communication and continuing self-education could be obtained by allowing interested students to assume control of their own learning in a setting using certain psychodynamic principles of group dynamics.

The objectives of Coppola and Gonnella share many similarities with the goals of a democratic education elaborated by Carl R. Rogers: "to help the student to become individuals who are able to take self-initiated action and to be responsible for those actions; who are capable of intelligent choices and self-direction; who are critical learners able to evaluate the contributions made by others; who have acquired knowledge relevant to the solution of problems; who work not for the approval of others but in terms of their socialized purposes."[5] Certainly these are attributes of a competent physician as well.

L.H.N.

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White Thrombus Prevention By Dipyridamole

The white thrombus which is found in areas of rapid blood flow, such as arteries and on prosthetic valves, appears to be composed of an aggregation of platelets in a fibrin mesh. Mustard et al[1] have described the histologic evolution of the white thrombus from its initiation as a platelet deposit to the formation of a fibrin mass. This unique thrombotic process is thought to arise chiefly from the action of ADP through mechanisms independent of blood coagulation. This is why anticoagulants whose action is directed primarily at plasma clotting factors have little effect on platelet thrombosis and probably explains the indifferent results of this kind of therapy in thrombotic diseases of the coronary and other arteries[2].

If the deposition of the blood platelets is the initiating factor in the formation of a white thrombus and has an important role in its propagation[3], then a compound that reduces the tendency of the blood platelets to aggregate should retard the initiation and propagation of thrombi in arterial walls as well as on prosthetic valves. The prevention of the latter type of thrombus can be readily studied in patients with prosthetic valves because of the relatively high incidence of thromboembolism is such cases. Sullivan et al[4] have reported encouraging results in just such patients. To their customary program of coumarin anticoagulation they have added dipyridamole, an agent previously shown to alter platelet behavior in vitro and in laboratory animals.

Dipyridamole is a coronary vasodilator, reduces spontaneous aggregation of platelets in saline solution. It alters electrophoretic mobility of platelets in rabbits in response to norepinephrin, diminishes platelet adhesiveness in patients with coronary heart disease and even reduces thrombus formation in wire meshes placed in the right atrium of a dog. At the time Sullivan et al began the use of dipyridamole in patients with prosthetic valves, this compound appeared to have the fewest undesirable side effects of all the compounds then known to influence platelet behavior with the possible exception of linolenic acid[5]. The mechanism by which dipyridamole actually reduces platelet adhesiveness and aggregation is unknown but may involve the fact that it inhibits the transport of adenosine across erythrocyte membranes to an intracellular site where it is ordinarily catalyzed by adenosine deaminase and that adenosine is known to reduce platelet adhesiveness.

Sullivan et al achieved total protection against embolism in 27 patients followed for at least one year after replacement of mitral or aortic valves. Of a comparable series receiving a placebo, arterial embolism occurred in 17 per cent and in 29 per cent in patients who discontinued dipyridamole.

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The authors tentative conclusion is that the addition of dipyridamole to a program of anticoagulation will reduce or eliminate embolic complications in patients who can tolerate a large dose of the drug. This series must now be enlarged and followed for a longer time before final conclusions can be reached.

Despite the limited number of patients and the sizeable group that had to discontinue the drug because of side effects, the results are impressive and reinforce an awakening interest in this and other drugs which can show equal success and no side effects when taken over long periods of time. Reduction of platelet aggregation has been claimed for acetylsalycilic acid, phenyl butazone, glyceryl guacolate, clofibrate and several other apparently unrelated compounds which now await clinical trial. The paper by Sullivan however appears to be the first demonstration that a drug operating against platelet adhesiveness has clinical efficiency as an antithrombotic agent.

If the protective effects of dipyridamole on platelet thrombus formation is further validated, it opens a new field for attempts to prevent arterial thrombosis which is such a potent cause of invalidism and death especially coronary thrombosis.

L.H.N.

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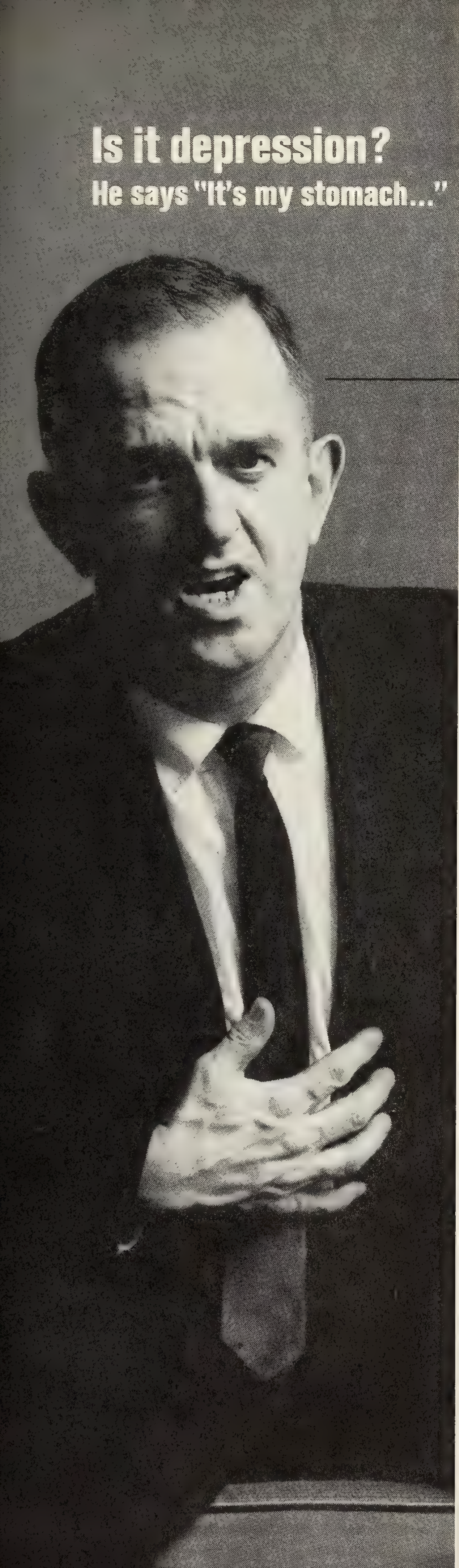
Present Status Of Enzymatic Thrombolysis: I. Streptokinase

The doctor is in need of a practical and effective form of clot-dissolving therapy that could be used for the rapid lysis of obstructive blood clots. At present there is no established medical means for directly influencing an existing thrombus or embolus. Anticoagulants although widely employed in medicine have as their primary goal the prevention of new clot formation but do not significantly influence a preformed thrombus. Furthermore, the arterial clot is essentially a mass of aggregated platelets formed on a denuded atheroma and consequently poorly responsive to even thrombolytic agents. In the case of the arterial thrombus agents operating to prevent platelet adhesiveness are therefore more likely to be effective than thrombolytic agents.

Thrombosis has become the prime health hazard of the adult population of the western world and an effective therapy could produce an enormous saving in morbidity and mortality. For this reason since 1958 this *Journal* has dealt recurrently with the growing number of studies on therapy in thrombotic disease[1-8] pointing out the state of our knowledge both in enzymatic and pharmacologic thrombolysis. The final accomplishment of these important therapeutic advances has been delayed for a number of reasons, the sparsity of agents worthy of testing and each with its own limitations, a lack of well trained clinical investigators interested in this project, the hazard of bleeding associated with intense thrombolytic states, controversies as to the best pharmacologic approach, and the increasing complexity of the trial necessary for establishing clinical effects.

The emphasis in developing a thrombolytic agent has been more on ways to accelerate the body's own mechanism for lysing thrombi and less on the search for pharmacologic agents that could do this, although much work has been done with phenylbutazone and dipyridamole in platelet thrombi. Venous thrombi however are uniquely adapted to undergo dissolution, for when they form they incorporate into their interstices a naturally occurring fibrinolytic enzyme system in the inactive form—plasminogen. In the presence of an activator or kinase, this plasminogen becomes converted into plasmin an enzyme capable of dissolving the fibrin of the clot, thus leading to its dissolution.

Plasmin if poured into the blood stream acts like trypsin, is proteolytic and can digest a variety of proteins, but inside the clot, plasmin has only fibrin available for digestion and there is little to inhibit the action of plasmin on fibrin. Normally the capillary bed contains much plasminogen as do the glandular ducts, the urinary tract, the prostate and the lungs. Thus whenever fibrin forms in the microcirculation, the activator along with plasminogen leads to rapid fibrinolysis, a mechanism that plays an important role in keeping the capillary bed free of obstructing fibrin deposits. Unfortunately not enough activator enters the circulation



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Careful observation of all patients is recommended. The antidepressant activity may be evident within 3 or 4 days or may take as long as 30 days to develop adequately, and lack of response sometimes occurs. Response to medication will vary according to severity as well as type of depression present. Elderly patients and adolescents can often be managed on lower dosage levels.

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to cope with large thrombotic masses that form in veins.

The demonstration that clot lysing ability of plasma was directly related to its activator content provided the impetus and approach for one form of practical therapeutic development in clot dissolution, the enzymatic method. To this area to date, of all agents tested, only the plasminogen activators streptokinase and urokinase have been found promising and then only when infused intravenously in appropriate dosage. The proteolytic enzymes acting directly on fibrin, including plasmin also lyse other proteins as well including the coagulation factors and are too hazardous.

Both streptokinase and urokinase are in the same phase of clinical investigation. Highly purified and adequately standardized preparations have been developed for patient use. Both agents produce a reasonably reproducible and sustained thrombolytic state that is well tolerated except for the problem of impaired hemostasis. This effect can be explained by their ability to degrade fibrinogen as well as fibrin. The induced thrombolytic state when sustained at several hundred fold over normal is capable of inciting lysis of human experimental as well as naturally occurring thromboemboli. What is needed now is to establish their efficacy in the treatment of disease by carefully controlled trials.

Streptokinase, produced by hemolytic streptococci, after fairly extensive investigation was dropped because of the tendency of such preparations to elicit undesirable pyrogenic reactions. There were a number of other problems. For example all individuals have a variable amount of circulating anti-streptokinase as a consequence of previous streptococcal infection and if this antibody is present it must first be neutralized before a level of free streptokinase could be maintained in the circulation. Accordingly the dose of streptokinase had to be individualized by preliminary titration of the patients plasma. Furthermore, careful monitoring of the fibrinolytic activity was necessary during the therapy to insure that the desired effect was being achieved in vivo. Another difficulty arose from its bacterial origin and treatment with it resulted in rapid immunization making its use for extended periods impractical. Finally there was an occasional severe allergic reaction to its use.

Despite these difficulties streptokinase has undergone extensive study in Europe where the agent has been commercially available for the past few years. Several of the problems mentioned above that led to its discontinuance in this country have been partly circumvented abroad, both the production of less toxic preparations, and the development of more arbitrary but useful dosage schedules. The European studies have amply confirmed the ability of streptokinase to dissolve intravascular clots and in a fairly large trial[9] testing its efficacy in acute myocardial infarction the mortality from this complication seemed to be halved. However, the protocol of this study had several serious weaknesses and the observations need confirmation, especially because they were studying the action of streptokinase on dissolving a platelet rather than a fibrin thrombus.

Despite the limitations inherent in the use of streptokinase, the fact that this agent can effctively produce thrombolysis in vivo and that its production, availability and cost pose no serious problem to the pharmaceutical industry suggests that full scale trials in well defined disorders should be instituted in the near future.

L.H.N.

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Present Status Of Enzymatic Thrombolysis. II. Urokinase

Urokinase is a naturally occurring activator present in human urine and made by the kidneys. This enzyme thus serves to keep the urinary tract free of fibrinous deposits. It possesses a number of virtues as a clot dissolving agent which are superior to streptokinase. It is of human origin, is nonantigenic, does not require individualization of dosage nor careful laboratory control as does streptokinase. Furthermore, it is considerably more fibrinolytic and less fibrinogenolytic than streptokinase.

However, to obtain it in sufficient quantities many problems had to be overcome. There was need for eliminating contaminating urinary thromboplastin. We needed assurance that the material would be non-toxic and when enough material became available for clinical use, there was the need for appropriate standards. Despite these unusual problems two major pharmaceutical firms (Abbott and Sterling-Winthrop) succeeded in preparing potent preparations of the activator from large quantities of fresh urine obtained from military installations. At the same time the National Heart Institute (NHI) set up a Committee on Thrombolytic Agents to advise the Institute on the developments in this field.

This Committee immendately identified urokinase as a most promising agent, quickly defined the problems to be surmounted and then set about to help solve them. They developed reproducible methods for the assay of urokinase and worked out a useful standard, the CTA, or Committee on Thrombolytic Agents unit. The Committee also defined the type of preparation that would be most suitable for clinical investigation, that is a preparation of high specific activity and purity, freedom from thromboplastic contaminants, heat treated at 60° C. for ten hours for virus inactivation and non-toxic and non-pyrogenic in animals. It finally recommended that the N.H.I. contract with the pharmaceutical firms for the purchase of material meeting these specifications.

The material that was made available for clinical investigation fulfilled its initial expectations. At appropriate dosage levels the infusion of urokinase in man raised the thrombolytic activity of plasma approximately 300 fold and this level of activity could be maintained at will by a sustained infusion of the agent. After termination of the infusion the clot-dissolving activity rapidly disappeared from the circulation. Because the level of thrombolytic activity was associated with a slower rate of plasminogen activation than that caused by streptokinase, there was also much less disturbance in plasma fibrinogen and anti-thrombin activity.

The thrombolytic activity maintained in the plasma was related to the dose of urokinase infused when calculated on a body weight basis with little variation among patients. Accordingly preliminary titration and rigid laboratory control was unnecessary. Currently a urokinase dosage that achieves thrombolytic activity approximately 300 times the normal was not found antigenic and no unexpected toxicity has been encountered. Johnson, McCarty and Newman[1] then established that intravenously administered urokinase could dissolve induced venous thrombi in the arm veins of human volunteers.

Fletcher et al[2] also carried out studies on patients with thromboembolic disorders and found urokinase successfully lysed clots occurring during the natural course of disease in about half of the cases. Now Sherry[3] reports a patient with retinal artery thrombosis in whom the clot appeared to be lysed by urokinase, another with severe iliofemoral thrombophletbitis with total dissolution of all the thrombotic masses and restoration of the circulation. He documents successful lysis of a paradoxical embolus in the left renal artery and in another case of multiple pulmonary emboli after infusion of urokinase for eight hours.

Such clinical observations are highly encouraging but many investigational problems remain. Why do some clots dissolve and others do not? Is it due to the age of the thrombus, a fact not always easy to establish? It is due to the nature of the perfusion of the involved segment as for example in arterial thrombosis? How active could

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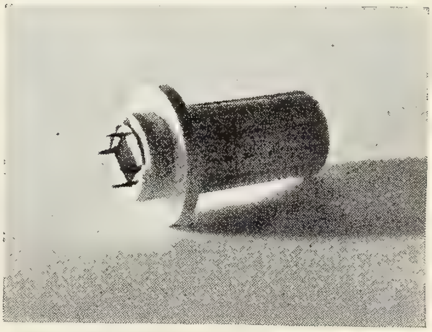

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such a fibrinolytic state be against a platelet rather than a fibrin thrombus? Then there remains the question of how to prevent bleeding often attending the infusion of urokinase both at the cut-down site as well as elsewhere. This especially is a problem that must be clarified and controlled if the agent is to be recommended for general use in the future.

During the past two years a number of investigators have been studying the natural course of pulmonary embolism by angiography, lung scanning and hemodynamic measurements because this lesion offers an excellent favorable model for the investigation of a thrombolytic agent. In the lung the perfusion in the area is high, the embolus is usually composed of recent blood clot, significant spontaneous resolution occurs and the underlying vessel is not damaged but most often normal. Fifty patients treated with urokinase were reported on at a conference held after the first year of experience[3]. Some showed striking resolution of emboli within a twenty-four hour period. Others were less impressive because perhaps the embolus was old. However, the experience was useful for delineating the direction of further investigation to provide quantitative data on resolution rates and morbidity comparing the effects of urokinase followed by heparin with that of heparin therapy alone.

If urokinase were to be able to lyse arterial thrombi then it would have its greatest usefulness especially in the management of acute myocardial infarction and cerebral thrombosis. However, there are many obivous reasons why the cerebral problem should be delayed and experience first gained with urokinase in acute myocardial infarction. This problem should now receive first priority.

If current projections are correct, the next few years should see carefully controlled trials carried out with streptokinase but especially with urokinase. The results of such trials should determine whether these particular enzymes will have a significant place in the therapy of thromboembolic disorders. There will still remain the search for pharmacologic agents particularly in dissolving platelet thrombi. Up to this time dipyridamole and phenylbutazone are the only drugs that have been shown to be successful in preventing and overcoming the platelet thrombus in small series of some patients.

L.H.N.

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Air Pollution: I. The Problem

Over the past fifty years development of industry, especially the chemical industry in and around cities, the growth of cities, and of motorizing transport have led to great increase in the amount of impurities in the air. At the same time the number of people exposed to these impurities have constantly risen through the shift of populations into towns. Any change in the purity of air a person breathes is of vital importance to him since any substances carried in the air, gases, vapors, particles, droplets measured in microns or less, which are not filtered in the upper respiratory tract are able to penetrate deep down in the alveoli of the lungs. If these substances are present in a high enough concentration, they can over a long period of time have local harmful effects, very often pass into the blood stream and give rise to toxic symptoms on blood vessels and nerve receptors[1].

Several questions therefore arise: (1) what are the sources and agents of air pollution, (2) what is the nature of the health hazards which can come about from air pollution, (3) ethical and moral questions arising from the right of every individual to clean air, such as to whom does the air belong, what right does anyone have to poison it for others, (4) what can those who are being poisoned do to preserve themselves, (5) what principles need to be followed to prevent air pollution.

There are four basic sources of chemical air pollution; domestic fires, industrial fires and furnaces burning of industrial wastes, and motor vehicle exhaust. Then there is the poisoning which each cigarette smoker perpetrates upon himself. This is a very large segment of our population who indulge in a sort of slow suicide, pleasurable perhaps but none the less lethal[2]. Finally are the polluted atmospheres in enclosed areas of factories around houses etc, in which individual workers breathe polluted air for many hours in each day.

Truhaut[1] points out that the part each of these sources play in the overall pollution problem varies depending upon where an individual is, the climate, amounts and type of heating. This obviously requires knowledge of the type and extent of industrial activity and density of motor vehicle traffic. In particular is the threat of riding behind a bus or truck for any length of time and being forced to breathe their exhaust in high concentration. The degree of responsibility borne by the motor car is obviously much higher in cities with congested vehicles using many millions of gallons of gasoline and oil per day. The domestic and industrial fires produce waste products of incomplete combustion as do also poorly adjusted carburetors and inefficient motors in automobiles and trucks and buses.

Coal and mineral oil contain a proportion of sulphur and their combustion products are constantly released into the atmosphere as SO_2 becomes SO_3 thence H_2SO_4 which remains suspended in the air in the form of minute droplets. Incomplete combustion also liberate CO instead of CO_2 and ashes, unburnt hydrocarbons such as 3-4 benzpyrene a powerful carcinogenic agent. In addition industrial wastes produce arsenical vapors, fluoride fumes and SO_2.

The exhaust gas from motor vehicles include CO, aldehydes, unburnt hydrocarbons, SO_2, small amounts of lead and most of all polycyclic aromatic hydrocarbons absorded by heavy unburnt particles which appear in the form of thick black smoke when diesel engines are badly adjusted. In general the nature and quantity of substances imperfectly burned determines the type and extent of the pollution. However meteorological factors also play an important part. On foggy days a real layer of sooty dirt settles on a car's windshield and this dirt can penetrate into the upper respiratory tract which can be detected by blowing ones nose. An even more unfavorable meteorological condition is provided by what is known as "temperature inversion" when a ceiling of warm air prevents any spread and traps the pollutants close to the ground[3].

If these consist of smoke mixed with fog we get "smog" a sort of persistent aerosol or micro mist which is particularly likely to get deep down into the bronchial tree. This sort of thing happens in many cities which are heavy consumers of solid or liquid fuels. If SO_2 is emitted it is burned to "acid smog" occurring especially in the winter foggy season.

When cities are situated in a sunny climate there may be photochemical reactions which change the nature of the pollutants originally emitted. In Los Angeles for example the NO_2 and carbonyl compounds resulting from the cracking of petroleum interact to give finally compounds of the peracetyl nitrate type and ozone. The air thus takes on both irritant and oxidyzing properties incorrectly termed "oxidyzing smog." Obviously the nature and direction of the wind have a major role in that they govern the way pollution spreads.

We can thus divide air pollutant hazards to health into immediate toxicity, long term toxicity and induction of malignant tumors. Immediate toxicity is often the result of short term exposure to relatively high concentration of pollutants particularly after a latent period of slow exposure. It is a health risk found in exceptional cases as the result of accidental emission of large quantities of pollutants or of particular meteorolgical conditions. Truhaut cites several such examples. In 1930 in the Valley of the Meuse 1,000 persons showed symptoms of poisoning and 60 died. In Donora, a small industrial town close to Pittsburgh, in October 1948, 6,000 persons were affected of whom 20 died. In London in 1952 and 1962 old people died by the thousands, the main toxic substances that were involved were SO_2 5.7 $mg./M^3$ and sulphuric acid. There was also widespread but much less harmful irritation of the mucosa of the eyes, throat and bronchi.

The long term toxicity comes about from exposure to substances having a cumulative effect. Fluorine bearing smoke from certain types of factories has caused fluorine poisoning in cattle because of contaminated cattle fodder. Prolonged exposure to sulphur pollution is likely to end in chronic bronchitis especially in cities like London which have an acid type of pollution. Long term inhalation of pollutants by cigarette smokers of course also leads to emphysema, chronic bronchitis and periods of CO poisoning.

Then of course is the induction of malignant tumors as a result of exposure to carcinogens like dimethyl aminoazobenzene, and diethylnitrosamine, polycyclic aromatic hydrocarbons, present in the heavy unburnt substances given off by domestic and industrial fires and by heavy motor vehicles. We cannot forget the chimney sweepers cancer of the scrotum known to be caused by soot. The benzpyrene compounds have been identified and measured in the air over innumerable industrial towns and found in very significant amounts: 3 mg./100 M^3 in Los Angeles, 2.4 to 14.7 in London[1]. The polycyclic aromatic hydrocarbons have been measured in the air over many other towns and their content depends upon the sources of pollution represented by different means of heating, higher in winter than in summer.

The dangers of carcinogen pollution are real, demonstrated both experimentally and statistically. Lung cancer has increased spectacularly over the past few decades in part due to better diagnosis, but mostly due to cigarette smoking and degree of pollution of air over industrialized cities. This relationship appears specifically to epidermoid and anaplastic types of bronchial cancer. The toxicological assessment of these health hazards are however complicated because we are really dealing with a sort of pollutant stew. Appraisal of the hazard involves study of exposure to an association of substances and admittedly these operate through various mechanisms both antagonistic and synergistic. For example light hydrocarbons released from autos and trucks and refineries act as solvents and eluants with respect to carcinogenic polycyclic hydrocarbons absorbed by soot particles thus exacerbating their harmful effects[4].

L.H.N.

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Dear Dr. Nahum:

I would like you to consider the following as a brief notation or "Letter to the Editor."

In our current era of heart transplants, one of the most vexing problems has been to establish the death of the donor. Many of the patients thus far selected have been said to have complete brain destruction, but with adequate heart action. The following case illustrates a young girl, deeply comatose, who presented with findings of (1) fixed dilated pupils, (2) complete areflexia, and (3) total apnea. In a recent symposium on organ transplants, these three items have been proposed as criteria of death, together with a flat EEG. The patient described below remained comatose with all these findings for 14 hours and did recover completely without any residual brain damage.

The patient is a 17-year-old white female who was admitted to Mt. Sinai Hospital, emergency room in deep coma. She was found to have fixed dilated pupils and was totally apneic. She was last noted to be conscious at 4 p.m. and was found unconscious at 8 p.m. on the day of admission. The family stated that she had been under psychiatric care in New York and had been taking Valium and Tofranil in the past. However, no empty bottles of drugs were found by the bedside and the family was completely unaware of what the patient might have taken in the way of drug dosage.

The patient's past history and review of systems were not available.

Physical examination revealed the patient to be deeply comatose. The pupils were fixed and dilated. The fundi were normal. Corneal reflexes were absent. Neurological examination revealed complete areflexia. The neck was supple. The chest was clear to percussion and auscultation. The heart revealed a sinus bradycardia with no murmurs and was not enlarged. The abdominal examination was negative. The extremities were completely flacid but otherwise normal. The remainder of the examination was non-contributory. Serum and urine blood levels for barbiturates and bromides were negative. A copious gastric lavage failed to reveal any further medication. The initial CBC, urine, blood chemistry and electrolytes were all normal. The patient's parents refused permission for electro-encephlogram.

On admission the patient was completely unresponsive. There was no history as to exactly how long she had been comatosed. There were no spontaneous respirations. The heart beat, however, was normal. Because of this an endotracheal tube was put in place and the patient started on positive pressure breathing. She was given 20 mg of Ritalin intravenously immediately and the Ritalin was given every one-half hour throughout the night. Patient was also started on Emivan and intravenous fluids. The dosage was 500 mg of emivan per 1,000 cc of fluid. The dosage was kept purposely low because of unknown cross reaction with Ritalin.

The patient was treated by me throughout the night. On three to four occasions attempts to remove the automatic respirator revealed that the patient still had no spontaneous respirations. Her pupils remained fixed and dilated. The corneal reflexes remained absent and she remained completely areflexic. The cardiac monitor continued to show normal heart action. She continued to have Ritalin every one-half hour. Approximately 14 hours after admission, the patient began to breathe spontaneously and the pupils became reactive. She slowly became responsive. Cardiac monitor at this time revealed a nodal tachycardia with multiple premature ventricular contractions. The Ritalin was stopped but she continued to have premature contractions, and then developed runs of ventricular tachycardia. Because of this a Lidocaine drip was started—2 gms to 1,000 cc of intravenous fluid. This completely abolished the arrhythmia and the drip was discontinued after four hours.

Subsequently the patient became completely lucid. She stated that she had taken approximately 30 chloralahydrate plus Sominex and Valium in unknown amounts. There was no residual brain damage.

The patient was discharged to the care of her psychiatrist.

Although an electro-encephlogram was not taken, this patient could have been pronounced dead by many criteria. In fact, she remained totally comatosed for 14 hours with complete apnea, and many observers felt that the patient was simply a heart-lung preparation. Because of this, renal dialysis was not considered realistic. The fact that this patient recovered without any residual evidence of intellectual impairment should make us extremely cautious about the present selection of donors-for transplants.

S. Richman, M.D., Director
Section of Cardiology
Mt. Sinai Hospital
Hartford, Connecticut

To the Editor:

Pediatricians frequently receive requests from preparatory schools or colleges for medical information concerning a patient who has been under care for many years. Many physicians are rightfully hesitant to send information of any consequence because the doctor's primary obligation is to maintain the confidentiality of the doctor-patient relationship. There is another important fact to consider when the medical report form is given to a physician with an envelope, addressed *To the Registrar* or *To the Admissions Office*. The possibility exists then for the confidential medical information to be handled by a series of officials and secretaries before it is finally filed in the medical director's office.

Thoughtful physicians, recognizing the possibility of a breach of confidence, usually send a very limited amount of medical data. The student and the college physician are thus at a disadvantage, for important information is unavailable to the doctor who is responsible for the student's health.

Dr. Robert Gage, Director of Health at the University of Massachusetts, and President-Elect of the American College Health Association, outlines in a letter to the Editor of the New England Journal of Medicine, (Vol. 279, p. 167-168—July 18, 1968), appropriate course of action in such instances. . .

Each college or preparatory school should have a physician who, as Director of Health, is responsible for the medical care of students. This doctor should be the only person to receive the personal physician's detailed and confidential report. This should be done only after discussing with the patient what is to be included in the report. With the permission of the patient, and the assurance that the confidential medical information is available only to a responsible physician, the pediatrician or family doctor is freer to be candid and detailed in his report. When the name of the medical director is unknown, it is worthwhile to write for this information before mailing the medical form.

Dr. Gage offers an important service by suggesting a procedure for handling this aspect of medical responsibility.

Morris A. Wessel, m.d.
New Haven, Connecticut

Dear Doctor Nahum:

As you know, I have been an admirer of Connecticut Medicine and especially your editorials for years. However, I cannot limit my reading of the Journal just to the editorials and so in reading the August issue I noticed the electrocardiogram of the month. These graphs were put on the page in a very peculiar sequence in that two different tracings were broken up and the A and B portions rather then two complete tracings in sequence.

Although I am only a gastroenterologist, I have had training as an internist and was amazed to find that I disagreed with the Q. T. intervals in Part A of this graph. I thought the Q. T. interval was over 40 while it was called 28. Would you mind re-reading this graph to see whether I was wrong?

Incidentally, I showed this Journal to two cardiologists in our community, both of whom felt that I was right in that in Part A there is not a short Q. T. interval.

The July issue of Connecticut Medicine shows some graphs which were prepared from Montefiore Hospital in New York, in the interpretation of which I fully agreed. However, must we get out of state tracings for our Journal? I am sure that I could guarantee at least one electrocardiogram a month from our own practice with its proper interpretation and of interesting and educational value.

Max Caplan, M.D.
Meriden, Conn.

Reply to Dr. Caplan:

Dr. Caplan has mistaken a large U wave due to hypokalemia for a part of the T-wave in his QT measurement. The graphs were purposely arranged in the sequence which Dr. Caplan found peculiar in order to make it easier to see the great contrast in each lead in the pre-op and post-op tracing.

Hyman M. Chernoff, M.D.
New Haven, Conn.

Foreword

WHAT'S NEW

Cardiovascular surgery is, without doubt, the most dynamic field in the surgical sciences today. Still in its infancy with many unknowns, there has been a certain solidification of knowledge in recent years. This edition of "Connecticut Medicine" is dedicated to presenting the current status of some of these topics in a concise manner. The distinguished authors who have joined with me in the preparation of this journal have attempted to separate "facts from fancy" and place the available knowledge on a realistic plane.

The developments in the area of myocardial revascularization, which holds so much hope for the future, still poses many problems. Improvements in microvascular surgical techniques whereby successful vascular anastomosis could be regularly anticipated in vessels one millimeter or less might revolutionize the field. The current status of direct and indirect revascularization of the myocardium, however, have much to offer patients with coronary artery disease.

Techniques in vascular reconstruction have developed such that a clearer understanding of expected results are now available. The indications and complications of those procedures are well described in this journal. The future holds, hopefully, an improvement in synthetic vascular prostheses, especially as applicable in the smaller arteries. While the larger cloth substitutes are excellent in their long-term function, much needs to be improved with prostheses less than five millimeters in diameter.

Pulmonary embolism has only recently been appreciated in probably its true perspective. Massive pulmonary embolism is not necessarily an indication for pulmonary embolectomy and the role of fibrinolytic agents and other forms of medical therapy are only now being understood. Certainly as with most disease processes, prevention is far preferable to treating pulmonary embolism after it occurs.

The prosthetic cardiac valve is accepted as a giant stride in the management of acquired heart disease. Already, however, a number of significant complications have developed which has lead to the use of homograft and even heterograft heart valves in the human subject. The possibilities of these more physiological substitutes improving the results of valve replacements appears encouraging in the face of early reports, but more work needs to be done in this area before definite answers are available.

More dramatic changes are in view, however, in the surgical management of heart disease and technically successful heart transplantation has already been achieved.

A great deal of investigation is currently being performed in the field of mechanical substitutes for the heart. Although here are perhaps the greatest unsolved problems, it would appear that in light of today's knowledge a successful mechanical heart may be available during the next decade.

H. C. Stansel, Jr., M.D., *Guest Editor*

Current Status of Prosthetic Heart Valve Surgery

H. C. Stansel, Jr., M.D.

The last decade has been marked by the development of practical prosthetic devices for the replacement of seriously diseased cardiac valves. It is fair to state that this has been the major contribution of recent years in the management of acquired heart disease. While there are a number of efficient and widely used prosthetic valves in use in various centers, the valves developed by Dr. Albert Starr and his associates are by far the most widely accepted. For this reason and because the author's experience is largely limited to the Starr prosthesis, the opinions expressed in this paper will refer only to these particular devices.

Indications

Because of the relatively short duration of experience in the use of these devices and the complications that already are apparent, it is recommended that strict indications be present before considering the use of any prosthetic valve[1]. Generally speaking, this involves cardiac failure that is not significantly responsive to the usual medical regimens. Also, in the case of aortic stenosis, syncope or angina pectoris not clearly due to coronary artery disease is accepted as indication for valve replacement.

Mitral Valve Disease

Pure mitral stenosis without significant calcification is still best treated, in the author's opinion, by closed mitral commissurotomy. However, with the presence of heavy calcium deposits in the valve leaflets, effective opening of these severely diseased structures is unlikely to produce good valve function. While the commissures may be widely opened by closed or open heart techniques, the immobility produced by the calcium deposits severely hinders valve action. Therefore, significant calcific mitral stenosis is almost always an indication for prosthetic valve replacement.

Pure mitral insufficiency when severe enough to produce symptoms of heart failure is usually best treated by valve replacement. While occasionally the insufficiency may be due to a congenital cleft or annular dilatation such that some form of valvuloplasty may be effective, this is the exception rather than the rule.

The majority of patients we see have combined lesions of mitral stenosis and insufficiency. The typical valve has some commissural fusion and shortening of the chordea tindinae with loss of valve substance, particularly of the septal leaflet.

In these lesions nothing short of valve replacement can hope to restore normal valve function.

Aortic Valve Disease

Symptomatic aortic stenosis is clearly a surgical disease because of the ominous prognosis associated with aortic stenosis and congestive heart failure, syncope or angina pectoris. In children and in the rare adult with noncalcific congenital aortic stenosis, simple commissurotomy under direct vision is effective in reducing the stenosis. The long-term results of this procedure is as yet unknown, but it is likely that many of these congenitally thickened leaflets will go on to develop the typical picture of calcific aortic stenosis. However, at the present time it is clear that commissurotomy when possible is preferrable to valve replacement.

Calcific aortic stenosis of significant degree is a definite indication for valve replacement. Surgical debridement of the calcific deposits, in vogue a few years ago, could produce good valve mobility and relief of the obstruction but adequate followup has confirmed the rapid redeposition of calcium in the leaflets and recurrence of severe aortic stenosis in most patients in two years or less.

Aortic insufficiency, even if severe, is a relative indication for valve replacement. It is well-known that this lesion is tolerated far better than severe aortic stenosis. Once symptoms of significant congestive failure appear, however, valve replacement is clearly indicated. While occasionally a perforation of a leaflet may be simply repaired, usually one finds very redundant leaflets associated with annular dilatation such that any form of valvuloplasty is ineffective in relieving the insufficiency.

DR. H. C. STANSEL, JR., Assistant Professor of Surgery, Yale University School of Medicine, 333 Cedar Street, New Haven.

As in the combined mitral valve lesion, the diseased aortic valve we usually find at surgery has elements of both severe calcific stenosis with some degree of insufficiency. It is for this type of valve that prosthetic replacement is clearly indicated.

Tricuspid Valve Disease

Diseases of the tricuspid valve where valve replacement is indicated is a highly controversial subject. Except for Ebstein's malformation of the tricuspid valve where a few authors have reported encouraging results with valve replacement, this subject remains unanswered. Most tricuspid valvular disease is secondary to severe mitral valve disease with resultant elevation of right ventricular pressure, dilatation of the right ventricle and subsequent tricuspid insufficiency. It appears clear that in most patients effective repair of the mitral valve lesion will lead to a fall in right ventricular pressures and a restoration of competency of the tricuspid valve. It is apparent, however, that some patients will not survive the postoperative period until the pulmonary vascular resistance falls sufficiently to permit a return to competence of the insufficient tricuspid valve. It is in these patients that tricuspid valve replacement appears indicated. While there is no absolute method to select these particular patients, the following procedure appears to be largely reliable. First, the mitral valve lesion is repaired, usually by means of valve replacement. The incisions in the heart are repaired and the heart-lung machine is turned off to evaluate the ability of the heart to maintain the circulation. If the heart is unable to maintain good circulatory dynamics, or if gross tricuspid insufficiency persists, then tricuspid valve replacement is carried out. Using these criteria only an occasional patient undergoing mitral valve replacement will need tricuspid replacement in spite of significant preoperative evidence of tricuspid insufficiency.

A word should be said regarding the relatively uncommon patient with rheumatic tricuspid stenosis. This lesion, due to loss of valve substance, almost never is repairable by simple commissurotomy and when present is usually best treated by tricuspid replacement.

Operative Mortality

The risks of valve replacement has progressively been lowered during the past few years. With the appreciation of the importance of postoperative respiratory support, temporary electrical pacemaking and prevention of air emboli, the operative mortality is now acceptable for most lesions. Isolated aortic valve replacements should have an operative mortality in the vicinity of five per cent at the present time. Replacement of the mitral valve is associated with a significantly higher risk probably because of the changes in the lungs and pulmonary vascular tree almost always seen with severe mitral valve disease. In most clinics the reported operative mortality for replacement of the mitral valve varies from 10 to 20 percent. The risks of multiple valve replacement varies widely in literature reports but it appears likely that as sicker patients are operated upon, the risks are correspondingly greater. In the author's experience this has certainly been the case and will probably hold true in most centers.

Complications

With at least six years of followup available in patients undergoing valve replacement, certain complications have developed. The most common has been embolization from thrombus formation about the prosthesis. In some of the early models of the valve the rate of embolization, especially from the mitral prosthesis was as high as 35 to 40 per cent. For this reason permanent anticoagulation with Coumadin was recommended in all patients undergoing valve replacement. It soon became apparent that the site of thrombus formation usually was the interface between the exposed metal of the valve cage and the cloth fixation ring. Subsequent improvements in valve design have lead to the current model in which the entire cage is completely covered in cloth so that tissue may invade and cover the entire prosthesis. Early reports would suggest that this change has largely eliminated the embolization problem. The author no longer anticoagulates any patient with the current valves and it is hoped that this complication has been solved.

Another significant complication with the early valves has been ball variance. This, as yet poorly understood phenomenon, is characterized by changes in the silicone rubber ball itself.[2,3] Apparently due to absorption by the ball of body constituents, there has been a change in its mechanical properties such that the ball changes shapes, fractures, or occasionally escapes from the cage, produces free aortic insufficiency, and usually rather sudden death. Although the exact incidence of this complication is as yet unknown, it is anticipated that at least 10 per cent and perhaps more of the silicone rubber balls will suffer this fate. Strangely, this complication has not been a factor in mitral or tricuspid valve replacements, being limited to the aortic valve. With the passage of time it is likely that a greater percentage of the aortic silicone rubber balls will undergo this degenerative change and require replacement. Starr has described a technique whereby he has been able to identify this ball variance by changes in the phonocardiogram before fatal valve function ensues. These abnormal valves then should be replaced with the newer models having hollow stellite metal balls which should solve this particular problem.

The most serious complication of the artificial heart valve and the one that remains largely unsolved is infection of the prosthesis. This tragic event occurs in about a six to eight per cent incidence. The organisms involved are usually a coagulase negative Staphylococcus albus although a variety of bacteria and fungi have been reported. The result of such infection is either massive thrombus formation about the valve or more commonly valve displacement and free regurgitation around the prosthesis. Attempts at massive antibiotic coverage and valve replacement have been made but usually with fatal results. There is good evidence to suggest that this complication can be minimized by meticulous sterile technique and prolonged prophylactic antibiotics but it is a most serious complication when it develops.

Results

It is apparent from the above discussion that there are many problems as yet unsolved with prosthetic heart valve replacement. While the operative mortality continues to decline, it is still significant, particularly with severe mitral valve disease. However, in those patients successfully undergoing valve replacement the results are dramatic. If one combines the operative mortality with those late deaths associated with one of the complications, there will be about 25 per cent of operated patients dead in two years. About 10 per cent will have only minimal improvement, probably because of associated myocardial disease. The remaining 65 per cent will demonstrate a return to essentially Class I cardiac status whereby they will be free of significant cardiorespiratory symptomatology. When one considers that these patients were all late Class III or Class IV cardiacs before surgery, the results are indeed gratifying.

Summary

The development of effective artificial prosthesis for severely diseased cardiac valves has revolutionized the management of acquired heart disease. The operative mortality is now within acceptable ranges although further improvement is clearly indicated. The major complications of embolization and ball variance may be solved although infection of the prosthesis remains a most serious problem. However, in those patients successfully undergoing prosthetic valve replacement, the results certainly justify the risks.

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Surgical Management of Arteriosclerosis Involving the Lower Extremities

Ormand C. Julian, M.D. and Hassan Najafi, M.D.

Arteriosclerosis obliterans is beyond doubt the most common human ailment. Surgical relief of the obstructions to arterial flow which it causes has been a reality for almost twenty years and tremendous effort has been expended by numerous surgical groups toward improvement and refinement throughout this period. If it could be said that all symptomatic arteriosclerosis could be corrected surgically, it would be important only to discuss the methods of diagnosis and the techniques of the operative procedure. The imperfections and limitations in this field, however, make it far more important to be knowledgeable of a selection of patients in order to avoid inappropriate surgery or inappropriate withholding of operation from patients who would benefit.

The possibilities and results of surgical interference, on the one hand, include complete abolition of obstruction and symptoms even in the most severe cases, while on the other they include serious worsening of the condition if the procedure fails either immediately at the time of operation or at a later date. The results are further affected by the fact that arteriosclerosis is a progressive condition and the underlying process is not fundamentally altered by the mechanical restoration of circulation.

It is the present purpose, therefore, to present a point of view concerning the selection of patients for surgical correction of aorto-iliac arteriosclerosis and of this lesion involving the femoral popliteal area as well as the smaller vessels below the knee. Indications for surgery are broadly based on the prognosis that can be made from the character of the symptoms and signs, and the anatomical location of the major obstruction as it is determined at first on the basis of physical examination and then refined through the critical use of x-ray visualization of the arteries. The former permits a fairly definite prediction of what will happen to the patient and his extremities if he is not operated upon, and the latter is a basis of prediction of the outcome of surgery and how long successful result will last.

Relation of Symptoms to Prognosis

In slowly progressive arterial insufficiency the first clinical manifestation is the development of symptoms during exercise, referred to as intermittent claudication. These symptoms come on when the amount of blood reaching the tissues becomes inadequate to supply the needs of walking and stair climbing, while at the same time it is quite adequate to supply the needs at rest. The patient may date the onset of the difficulty to a very specific episode involving stair climbing or running. He learns that he can walk at a slower pace without symptoms, but that the distress will recur when he again undertakes the heavier activity. Sometimes an improvement is experienced for a period after such an onset and, during this phase of the disease, abstinence from smoking, weight loss and a regime of progressive exercise is effective. More often the severity of the intermittent claudication increases progressively and it becomes more easily elicited by lesser amounts of exercise.

This kind of onset reflects a slowly developing arterial insufficiency which it has been uncovered on the day of onset of symptoms simply by the fact that the patient has undertaken activity which is greater than that which is usual for him. In this case one would say that the time of onset reflects the activity of the patient rather than any real change in the arterial lesions.

Another kind of rapid or even abrupt onset is one in which the first symptoms occur during either rest or exercise of any degree. The development during the course of a chronically progressive arteriosclerotic occlusion is caused by the sudden thrombosis of narrowed segments of the blood vessel. The severity of the symptoms at the be-

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ginning is variable depending upon the size of the lumen which had been maintained up until the time of the acute occlusion. This reasoning is based on the concept that arteriosclerosis gradually occludes an artery by the creation of atheroma and perhaps mural clot up to a certain point, and that the remainder of the lumen is suddenly closed by a thrombus. During the development of the pre-occlusion stenosis, collateral circulation has kept pace with the slowly increasing obstruction. Review of the character of the onset and the early course of individual cases shows that it usually relates to the size of the remaining lumen at the time of the final thrombosis. If this lumen is large and the symptoms that result are severe and unremitting, the management must be that of an acute arterial occlusion. If the lumen is small and therefore the symptoms increase only moderately, the patient should be managed for his chronic arterial insufficiency.

There is a certain tendency for the symptoms in chronic arterial occlusion to progress in a step-wise fashion, rather than along a continuous curve of severity. A point of great prognostic significance is the development of symptoms of any kind without exercise. The patient passes into an entirely different class when this so-called rest pain, which occurs at the distal part of the extremity and has a neuritic quality, develops. The need for immediate consideration for treatment becomes absolute rather than a matter of choice.

The stage of symptoms becomes even more serious from a prognostic point of view when peripheral ulceration develops, either spontaneously or as a result of failure to heal of a small traumatic lesion.

As the symptoms become more severe there are certain changes in the signs exhibited by the extremity. Early in the course of the disease, when only intermittent claudication is present, the skin of the feet including the toes usually remains entirely normal in regard to color, temperature and texture. Serious and rapid progression seems rarely to be imminent during the time in which this low level of objective evidence of ischemia persists. As the interference with blood supply increases there is a progressive increase in the pallor exhibited by the skin on elevation and of rubor on dependency of the extremity. Progressive atrophy of the skin and small muscles of the foot begins and ulceration must be considered to be imminent. Edema of the extremity is a significant sign. The cause is not primarily the arterial insufficiency, but the edema is a secondary result of the fact that the pain of ischemia becomes more severe during elevation and is somewhat relieved during dependency. Consequently, an individual in this stage of the disease is likely to take and maintain a position in which the leg is dependent, and swelling results.

The signs elicited upon examining the extremity for pulses and the presence or absence of bruits audible with the stethoscope are less significant in determining the prognosis than they are in determining operability. Since, as will be noted later, direct surgical repair of the vessels below the knee is relatively unsatisfactory, the prognosis is serious in the patient with severe symptoms and other signs of arterial insufficiency who has femoral and popliteal pulses.

Physical Evidence of the Site of the Lesion

The severity of the symptoms and the presence of the ischemic signs are taken as indications of the degree of need for surgical intervention. The location of the arterial lesions determines feasibility and predicts results of the operation. Although the detailed information needed for actually mapping out the sites of obstruction will sooner or later be determined by arteriography in any given case, a very close approximation can usually be obtained by consideration of the findings as to pulse and the presence of bruits. In evaluating the anatomic character of the lesion by physical examination it must be kept in mind that, although arteriosclerosis is a generalized condition, it has a decided tendency to form localized segments of obstruction. In the lower extremities the obstructive lesions are most often found at the major branches: that is, the aortic, common iliac, common femoral, and popliteal bifurcations. One additional site of selection of obstruction is the point at which the superficial femoral artery passes the adductor tendon. The artery above and below a point of complete occlusion is rarely normal, and there are frequent individual instances of more than one occlusion. A further point of great importance is the presence of diffuse changes involving the branches of the popliteal artery and the smaller arteries of the ankle and foot.

Determination of the levels at which pulses are absent and at which bruits can be heard generally maps out the distribution of the occluding process and is the first step in deciding whether operation should be considered or not. A localized or diffuse stenosis without actual occlusion can very well produce symptoms. In many such instances the pulses may be easily felt down to the popliteal level, and even faintly perceptible at the ankle. Since absolute normalcy of pulse amplitude cannot be determined by palpation alone, the fact that such stenoses will produce an audible bruit and very often will cause an asymmetry of the amplitude of the palpable pulse is most important.

Several specific situations relating anatomical lesions to physical findings can be described. One of these is seen in a complete occlusion of the aortic bifurcation. The completeness of the occlusion makes it unlikely that a bruit will be heard in the iliac fossa or over the femoral triangle. However, the complete occlusion does not always ablate the pulses at the femoral level because pulses can be transmitted in the presence of an abundant collateral blood flow.

Second, involvement at the aortic bifurcation which causes complete occlusion of one iliac artery and stenosis of the other will almost ertainly be represented by a pulse and a bruit on the unoccluded side, and a faint pulse by way of the collaterals but no bruit on the obstructed side.

In connection with both of these situations, namely that with complete occlusion at the aortic bifurcation and aortic bifurcation disease associated with occlusion on one iliac and not of the other, the interpretation can be extended by considering the symptoms and signs described in the earlier section. It is unusual for chronically developing aorto-iliac occlusion either to cause more symptoms than intermittent claudication or to alter the nutritive balance of the skin of the foot or feet. Therefore, absence of pulses at the femoral level or the presence of only a collateral femoral pulse in a patient whose only symptom is intermittent claudication, and who has normal nutrition of the feet indicates an isolated aortic bifurcation lesion. One more extension can be made of this reasoning with considerable accuracy. This is based on the fact that femoral artery lesions are likely to be symmetrical. Therefore, when a faint pulse is palpable at the ankle on the side of incomplete iliac occlusion in aorto-iliac disease, it can be reasoned not only that the femoral popliteal system (including the vessels below the knee) are open on the side having the pulse, but also that they are likely to be open on the contra-lateral side.

A third combination which is subject to some detailed evaluation is that in which the femoral pulses are symmetrical and within a normal range and no pulse exists on either side below this point. The immediate inference is that the superficial femoral artery is occluded bilaterally, and in this situation the absence of any symptom other than claudication and the existence of normal nutrition suggests that neither common femoral bifurcation nor the popliteal artery segment and its bifurcation is occluded. Therefore, the lesion most likely to exist is an adductor canal lesion from which the occlusion may well have extended upward to the femoral bifurcation, not, however, embarrassing flow in the profunda femoris artery. A sub-class of this lesion in which the obstruction on one or both sides is incomplete, is that represented in patients who exhibit a bruit over the course of the superficial femoral artery at the junction of the lower and middle thirds of the thigh. The absence of bruits above in the femoral triangle while the pulses here are strong and symmetrical strongly supports the idea that the aortic bifurcation and the iliac arteries are normal.

The fourth combination, and unfortunately a very common one, indicates a diffuse distribution of aorto-iliac, femoral and popliteal changes. Occlusions or stenoses are present at several levels, and when the limb is pulseless, as it was in some of the previously described combinations, the differentiating factor is the presence of rest pain and signs of inadequate nutrition of the foot. Bruits may be present at several levels in the femoral triangle and thigh, as well as over the iliac fossa when this diffuse distribution has not produced proximal occlusion. Hope for successful surgical management in these situations depends largely upon the patency of the profunda femoris artery. If the profunda femoris is patent it is frequently possible to restore blood flow by a "profunda revascularization" operation, which will be described later. Physical examination alone cannot be predictive of whether the profunda branch is open or not. Very often aortography also fails to give us satisfactory and complete answers to this question, and operability is finally determinable only by direct exploration of the femoral artery bifurcation.

Results to be Expected of Reconstructive Surgery

Experience with reconstructive arterial surgery in the several varieties of aorto-iliac, femoral, and popliteal distribution which have been discussed makes it possible to predict with some accuracy the likelihood of success of the several available procedures. The statements concerning each can be taken to be basic. It is the opinion in our center that these statements should be quite rigidly applied in instances in which the symptom level is mild to moderate, particularly if symptoms do not interfere with the ability of the patient to carry on needed functions. On the other hand, rigid application of these criteria would be inappropriate in patients whose symptoms are severe and handicapping. A helpless and defeated attitude would be restrictive to improvement in the surgical armamentarium.

The important points can be stated briefly as follows:

1. The repair of an isolated occlusion in the region of the aortic bifurcation is virtually certain of immediate success and continued function.
2. The repair of an isolated occlusion of the superficial femoral artery in the presence of little involvement of the popliteal bifurcation produces an excellent result if the long saphenous vein of the patient is available as a graft.
3. Long reconstructions extending from the iliac artery to the distal femoral or popliteal artery will often produce initial success. There is a significant rate of late failure, particularly if a prosthetic bypass has been used. Since the late failure is virtually always acute and occurs after the previously developed collateral circulation has atrophied, the penalty is severe.
4. Reconstructions of the popliteal artery at its bifurcation and any portion of the distal branches are difficult and experimental procedures.
5. The combination of aorto-iliac or iliac obstructions with advanced disease of the superficial femoral artery can be treated successfully by a repair or a bypass extending from the aorta down to the bifurcation of the femoral artery, if the profunda femoris branch is open. The latter vessel is notably often spared by the disease process and it can receive blood through the reconstruction and pass it on through its distal collateral connections.

We believe that reconstructive procedures should not be done in cases that show extensive involvement at several levels, unless there is pain at rest or a degree of claudication which very seriously inhibits the patient's ability to follow his occupation. Another contraindication is the involvement of the greater portion of the superficial femoral artery when a prosthesis is required because the saphenous vein cannot serve as an autogenous graft. This contraindication is also disregarded if there are signs and symptoms of limb threatening type.

Surgical Procedures for Aorto-Iliac Lesions

An aortogram done by the translumbar route will usually define the extent of the disease in the aorto-iliac region for which an operation must be planned. It will also more often than not outline the ilio-femoral segment distal to the obstruction, showing more or less exactly where the distal end of the reconstructive procedure must be. Sometimes visualization of the distal vessels is unsatisfactory to this purpose, and it may be necessary to explore the femoral vessels to determine the amount of disease present at that level. The principle of carrying the operation from an open aorta above down to a point at which the vessel has a satisfactory lumen can never be ignored. The immediate restoration of pulses in the extremities is of paramount importance.

There are two methods of dealing with the obstruction in the aorto-iliac region. These are the implantation of a graft and the removal of an occluding atheroma and clot by thrombo-endarterectomy. Both woven and knitted grafts are used. The only material commonly in use at this time is dacron. Thrombo-endarterectomy is a somewhat more lengthy procedure but has the advantage of avoiding the implantation of artificial material. Experience has failed to indicate that either method of dealing with the obstruction is very much superior to the other once successfully accomplished.

The selection of the type of operation depends largely upon the character of the vessel and the extent of the lesion. When the vessel is of normal size and the arterial wall is not severely calcified for a localized lesion, a thrombo-endarterectomy is often used. Poor and obese patients may be given the advantage of a relatively briefer operation by using a graft. A graft is distinctly indicated if the aorta or the iliac branches are very much narrowed in outside diameter, or if there is an early stage of aneurysm formation.

When a graft is used palpation of the aorta after exposure at surgery aids in deciding what kind of anastomosis should be made between vessel and graft proximal to the obstruction. If the aortic wall is extensively diseased at the level to which the graft must be sutured, it is desirable to transect the vessel completely and make the anastomosis end to end. Another advantage of the end to end anastomosis is that mural clots and loose atheromatous material may be more thoroughly removed from the aorta just above the point of anastomosis. The advantage of an end to side anastomosis, which is done if the aorta is more nearly normal, is that a large connection can be made more quickly and with less dissection. The distal anastomoses are almost always made by end to side anastomosis.

In spite of all careful preoperative examinations, it is sometimes found that the common iliac or external iliac arteries within the abdomen where the anastomosis was planned prove to be unsatisfactory for this purpose. Therefore, in preparation for the operation, both lower extremities are completely prepared and draped in addition to the abdomen.

In the common situation in which aorto-iliac disease exists with significant involvement of the femoral artery system, several methods are available for making the distal anastomosis or of extending the bypass. The distal end of the graft may be extended by adding to it with an anastomosis another straight tube of woven dacron material of the same size. If necessary, this can be carried down as far as the bifurcation of the popliteal artery. Much more often, and certainly by choice, the distal anastomosis is made in the femoral triangle in such a way as to deliver blood only to the profunda femoris branch of the common femoral artery. This can be accomplished by an end to side anastomosis to the common femoral near the origin of the profunda branch.

When the graft must be extended outside the abdomen, either because the iliac vessels within the pelvis show an unexpectedly advanced state of change or as a part of the preoperative plan, the graft is tunneled retroperitoneally down to and then under the inguinal ligament. It passes under the ligament adjacent to the femoral artery, and the connection is made in the femoral triangle. This extension into the femoral region may produce a remarkable improvement even when the superficial femoral artery is closed. The so-called profunda revascularization that is accomplished causes the branches of the profunda artery to serve as a distributing complex of blood that now comes through the graft from a strong aortic source above, rather than from collateral pelvic branches which are relatively less adequate. Extension of the graft to the popliteal area is reserved for extremities having a very poor prognosis in which the profunda femoris artery is not available for profunda revascularization.

Reconstruction of the Superficial Femoral Artery

The procedure of choice for the reconstruction of the superficial femoral artery is a bypass graft, using the patient's saphenous vein. The presence of a saphenous vein satisfactory for a graft is one of the strong factors governing the success of a reconstruction on the femoral artery. The length of the obstruction and the character of the popliteal artery and its branches are other factors.

The saphenous vein is taken for a graft by direct exposure. It must be carefully cleared of the superficial layers of the adventitia and the tributaries ligated as the vein is dissected from its bed. During the dissection the vein is almost always seen to go into spasm, which is overcome by distending it with saline, using a syringe and manual pressure.

In the absence of a satisfactory saphenous vein, the prosthesis of choice is a woven or knitted dacron prosthesis. One which is eight millimeters in diameter is usually chosen.

When a saphenous vein type of bypass is used in patients whose vessels at the point of distal anastomosis and thereon below the knee are in good condition, the restoration of pulses that results is usually lasting. Our own experience with prostheses leads us to avoid bypass surgery in patients who do not have a satisfactory vein unless the symptoms surely warrant it.

Thrombo-endarterectomy can be used in the femoral artery and many be the procedure of choice when the artery has a relatively large outside diameter and is not extensively calcified.

The removal of the diseased inner portions of the media and the intima is done by a variety of methods. The entire occluded segment may be opened longitudinally and repaired after removing the diseased tissue, or the artery may be cleared out blindly using a long handled loop instrument. The open method requires much wider exposure of the femoral artery and is a prolonged procedure because of the length of the suture line required in repair. An opened up segment of autogenous vein is sometimes used to patch this long incision in order to enlarge the artery. This is even more time consuming because two suture lines are required.

Although it seems unwarranted to apply an extensive operative procedure for anything less than very severe symptoms, there is no such limitation to attempts of salvaging an extremity, the loss of which from arterial insufficiency is predictable.

Any of the revascularization procedures can be used in an attempt to prevent such loss. If an amputation seems imminent, it should in most instances be preceded by exploration of the vessels at the appropriate levels to rule out the possibility that the circulation can be restored. Occasionally a simple bypass or the relatively simple profunda femoris revascularization is applicable. More often, difficult small vessel repair below the knee will be necessary. Occasionally the posterior tibial artery is patent distally and can be used to receive the distal anastomosis as a limb-salvaging procedure.

Some other unusual techniques have developed and find use for salvage. In one a new arterial blood supply is brought from the axillary artery by way of a dacron graft tunneled under the skin of the thorax and abdomen down to the femoral bifurcation. This procedure and one in which a graft traverses the subcutaneous tissue above the pubis connecting the two femoral arteries can both be done under local anesthesia. In such instances general anesthesia and laparotomy are avoided, and occasionally good results are derived.

Lumbar Sympathectomy

Lumbar sympathectomy is useful in patients with distressing symptoms whose arteries cannot be repaired by direct methods. The best example is the patient suffering from an ischemic foot caused by infra-popliteal small arterial occlusions. Sympathectomy usually relieves the rest pain and may prolong the longevity of the limb. It is also used in conjunction with reconstructive surgery. For instance, when severe aortoiliac disease is associated with superficial femoral occlusion. Under these circumstances, if feasible, a dacron bifurcation graft to restore flow to the profunda femoris and lumbar sympathetomy is added to augment the collateral flow to the distal limb.

The most direct result of lumbar sympathecomy is due to its maximum effect on the vessels in the skin in the distal part of the extremity. It is not unusual for a sympathectomy to produce healing of a previously chronic ischemic ulcer. The greatest benefit results when sympathectomy is applied to patients whose sympathetic tone can be judged to be quite active on the basis of normal or increased moisture of the skin of the foot. It is least effective in diabetics, in which the diabetic neuritic involvement of sympathetic fibers has produced dryness of the skin. Atrophy of the skin and of the small muscles is virtually a contraindication. It is never used for the primary purpose of relieving intermittent claudication, although it frequently but unpredictably does improve the patient's ability to walk.

Conclusion

The amenability of arterial occlusive disease to reconstructive surgery is in part due to the pathologic characteristics of this disease entity. Whatever the mechanism responsible for the pathogenesis of arteriosclerosis, the process has a tendency of focal accentuation in certain areas of the arterial tree. In the absence of advanced disease in the arteries proximal and distal to the obstruction, restoration of flow to the affected extremity becomes technically feasible through the careful utilization of well established vascular procedures. The far more important consideration is the proper selection of patients for such arterial operations. In this connection, it should be emphasized that an asymptomatic patient or one who has a trival complaint is not a good candidate for surgery, even in the presence of a major arterial obstruction.

On the other hand, if the loss of an extremity is imminent maximum surgical efforts directed toward the improvement of circulation, and therefore salvage of the limb, should be undertaken.

There are certain contraindications to direct arterial surgery for the lower extremities. These include patients with far advanced lesions, such as gangrene of a major portion of the foot, those who have significant symptoms but in addition suffer from cerebral, coronary or renal impairments, and finally, the patients in whom inoperability can be determined on arteriography.

The most important duty of the surgeon is to determine the relative significance of the patient's symptoms and signs in terms of prognosis of the extremity. The presence of symptoms and of technically remediable arterial lesions do not in themselves constitute indication for surgery. These factors must be weighed against the degree of disability caused by intermittent claudication or the threat of loss of limb, as well as the magnitude of the operative risk, both to the involved extremity and to the patient's life.

The Diagnosis and Management of Pulmonary Embolism

Robert H. Jones, M.D. and David C. Sabiston, Jr., M.D.

Blood filtration is an important physiologic function of the pulmonary circulation[1]. The lungs retain and resolve small thrombi and recent evidence has shown that this resolution can occur with amazing rapidity. Unnoticed episodes of pulmonary embolism very likely occur throughout life especially during periods of inactivity and tissue injury which predispose to venous thrombosis. Massive embolism, especially of sudden onset overwhelms the functional reserve of the lungs causing a serious and often fatal disorder. Rudolf Virchow convincingly demonstrated this pathologic process more than a century ago[2]. Subsequent investigators have defined physiologic mechanisms underlying the clinical manifestations of pulmonary embolism. The recent introduction of specific preventive and therapeutic methods has prompted refinement of diagnostic procedures[3]. Yet, these important contributions have failed to decrease significantly the incidence or mortality of this disease. The magnitude of the problem is emphasized by pathologic evidence which has shown that pulmonary embolism can be demonstrated in over 60 percent of adults dying from all causes[4]. In a recent postmortem study from the Peter Bent Brigham Hospital, pulmonary embolism was found to be the leading cause of death[5]. A clinical diagnosis of this common disorder is not made in more than half of fatal cases due primarily to lack of sufficient suspicion and thoroughness by physicians. Application of a diagnostic protocol to all patients with symptoms suggestive of pulmonary embolism has been shown to increase the diagnostic accuracy from 30 to 70 percent the fatal cases recognized clinically[6]. The effectiveness of such a measure emphasizes the importance of a systematic approach to diagnosis and treatment of this disorder based upon a clear understanding of the basic pathophysiology of pulmonary embolism.

Pathophysiology

Circulatory Alterations

The venous thrombosis which precedes pulmonary embolism usually occurs in veins of the legs or pelvis. The high incidence of pulmonary embolism in patients with other thrombotic disorders suggests that all thrombi may arise by a common process, but intensive investigation has not revealed a pathologic mechanism basic to all thrombosis[7]. Clinical factors which facilitate venous thrombosis are stasis, vascular injury, and increased blood coagulability. Maturation or mechanical forces dislodge the venous thrombi. Such thrombi may pass through the heart intact, but often cardiac contraction fractures the thrombi and impacts fragments into the pulmonary arteries and arterioles.

Massive pulmonary embolism, especially when abrupt, increases pulmonary arterial pressure. Emboli lodging in arterioles 20 to 100 microns in diameter initiate transient reflex vasoconstriction of nearby pulmonary arterioles[8]. In the clinical situations the effect of reflex vasoconstriction on pulmonary arterial pressure is small compared to the increase in pressure from mechanical obstruction of pulmonary arteries. Elevated right ventricular systolic pressure matches the increased pulmonary vascular resistance in an effort to maintain pulmonary blood flow. Increased right coronary artery perfusion supports the added right ventricular work. A normal heart withstands 60 percent occlusion of the pulmonary circulation for extended periods without failure.[9]. Cardiac or pulmonary disease in patients reduces tolerance to pulmonary arterial occlusion, and a small embolic insult may be fatal to patients with severe underlying cardiorespiratory disease. When pulmonary arterial occlusion exceeds the capacity of an individual patient to compensate, heart failure rapidly ensues. Right ventricular diastolic pressure elevation, which marks the onset of heart failure, is manifested clinically by increased central venous pressure. Cardiac output diminishes and in both ventricles systolic pressure falls as the diastolic pressure rises. Systemic arterial hypotension reduces coronary perfusion. The heart dilates in ventri-

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cular fibrillation or arrest. If pulmonary embolism is not fatal, in situ thrombosis forms distal and proximal to the embolus in obstructed arteries[10]. Despite interruption of pulmonary arterial flow, the lung becomes infarcted in only a small proportion of patients (about 10%) due to the continuation of bronchial blood flow[11]. When infarction does occur it is usually found in association with either congestive heart failure or pulmonary suppuration. Within a week after experimental thromboembolism, blood flow resumes through the previously occluded pulmonary arteries and within a month a fibrous subintimal plaque represents the only residuum of the arterial occlusion[12]. In the presence of pre-existing cardiac or pulmonary disease, this poorly understood process of thrombus resolution occurs but is less rapid in such patients following pulmonary embolism and hinders restoration of lung function[13 14]. Thus, embolism of congested lung tissue may cause pulmonary infarction which does not resolve but which heals with scar tissue. Experimental evidence suggests that pulmonary edema occasionally observed in patients with pulmonary embolism results from infarction and is unrelated to pulmonary arterial pressure elevation[15]. Pulmonary infarction inconsistently activates a sympathetic reflex which increases capillary permeability throughout both lungs causing pulmonary edema. or unknown reasons, only a portion of patients with pulmonary infarction develop pulmonary edema.

Respiratory Alterations

Pulmonary embolism commonly causes dyspnea with rapid, shallow breathing. Mechanical stimulation of receptors in pulmonary arterioles initates this ventilatory reflex which is mediated through the vagus nerves. The quantity but not the distribution pattern of pulmonary arteriolar emboli determines the severity of reflex tachypnea[16]. Ventilatory changes may follow episodes of embolism which are too minor to elevate pulmonary arterial pressure[17]. The sensitivity of this reflex explains why dyspnea is the most frequent, and is often the sole clinical indication of pulmonary embolism. Dyspnea manifested by deep, labored breathing occurs in patients with massive embolism of large pulmonary arteries, but mechanisms responsible for this hyperpnea are unclear. Obstruction of major pulmonary arteries constricts corresponding bronchi[18]. Decreased carbon dioxide in ventilated lobes deprived of pulmonary arterial perfusion causes bronchoconstriction which can be relieved by restoration of a normal carbon dioxide concentration in affected bronchi. Bronchoconstriction partially corrects the ventilation-perfusion imbalance that follows embolism of large pulmonary arteries. Emboli to the smaller arteries and arterioles scattered throughout the lung cause diffuse bronchiolar constriction which is not influenced by carbon dioxide concentration. Serotonin released from fresh platelets adhering to emboli may cause bronchiolar constriction which can be prevented or reversed by administration of a serotonin antagonist[19 20]. Heparin prevents bronchiolar constriction by blocking serotonin release from platelets. Mild hypoxemia commonly follows pulmonary embolism and in 20 percent of patients is sufficiently severe to cause cyanosis. Unless pulmonary edema occurs, the slight depression of diffusing capacity after pulmonary embolism is not an important cause of hypoxemia. Mechanisms preventing complete oxygenation of blood after pulmonary embolism remain obscure. Although it is a potent pulmonary arteriolar vasoconstrictor and an activator of systemic chemoreceptors, hypoxemia is not a stimulus for circulatory or ventilatory alterations of pulmonary embolism.

Diagnosis

Clinical Manifestations

The magnitude of embolism and cardiorespiratory status determine the nature and severity of clinical manifestations of pulmonary embolism in individual patients. *Dyspnea is the most common manifestation in patients with pulmonary embolism*[6]. Other frequent abnormalities include tachycardia, tachypnea, accentuation of the pulmonary second sound, and rales. Only a third of patients with pulmonary embolism demonstrate clinical evidence of venous thrombosis. Dilation of cervical veins and an enlarged and pulsating liver indicate heart failure which if severe may cause cardiac arrhythmias, systemic hypotension, or anginal chest pain. Hemoptysis, pleural friction rub, pleuritic chest pain and chest splinting may follow. However, a majority of patients with pulmonary embolism show no sign of progressive heart failure, infarction, or cyanosis. The paucity of symptoms specific for pulmonary embolism demands that careful attention be paid suggestive signs especially in patients with conditions which predispose to embolism. In the absence of infarction, chest film findings may be suggestive but not diagnostic of pulmonary embolism. Pulmonary infarction is displayed on chest film by a half spindle shaped density based upon a pleural surface[21]. The most helpful cardiographic sign present in the plain chest film of pulmonary embolism without infarction is decreased or absent pulmonary vascular markings distal to the occlusion with correspondingly prominent vascular markings in uninvolved areas.

Other chest film abnormalities indicative of pulmonary embolism are atelectasis, pleural effusion and dilation of the right heart or major pulmonary arteries. However, it must be emphasized that the chest film of many patients with pulmonary embolism appears quite normal, especially in the early stages, and it is of diagnostic value only in confirming the absence of other pulmonary disease. Less than a fourth of patients with pulmonary embolism have abnormal electrocardiograms. When present, the abnormalities associated with pulmonary embolism include S-T segment depression, atrial arrhythmias, right axis deviation, prominent P waves, right bundle branch block and inversion of T waves in right precordial leads[22]. These changes are often difficult to separate from alterations due to the cardiac disease coexisting in many patients with pulmonary embolism. The most important function of the electrocardiogram is the aid obtained in excluding the possibility of myocardial infarction. Determination of serum levels of lactic dehydrogenase activity (LDH), glutamic oxaloacetic transaminase activity (SGOT), and bilirubin has been used in diagnosis of pulmonary embolism. About 75 percent of patients with pulmonary embolism develop abnormally high serum values of one or more of these factors[6]. The most frequent combination of alterations after pulmonary embolism is elevated LDH with normal SGOT and bilirubin. Elevation of both LDH and bilirubin is common after embolism in patients with heart failure. Inherent delay and inconsistent results make these serum determinations of little value as diagnostic tests for pulmonary embolism. In the absence of pulmonary infarction, the definitive diagnosis of pulmonary embolism requires specific diagnostic tests, and recognition of clinical manifestations suggestive of pulmonary embolism is essential for proper application of these procedures[23].

Specific Diagnostic Procedures

Pulmonary scanning quantitates alterations in regional pulmonary perfusion caused by any disease mechanism[24 25]. Aggregated radioactive human serum albumin is injected intravenously and particles lodge in pulmonary arterioles and capillaries with a distribution proportional to regional blood flow. Lung scanning inflicts minimal risk and discomfort to patients and is a sensitive indicator of regional pulmonary embolism. In the absence of other abnormalities on chest film, a perfusion defect on lung scan indicates pulmonary embolism. Since many diseases other than pulmonary embolism alter regional pulmonary perfusion, it is essential that the scan be interpreted in association with a simultaneous chest film. Pulmonary arteriography is an additional definitive diagnostic test for pulmonary embolism[26]. Although intravenous injection of dye occasionally produces satisfactory pulmonary arteriograms, dye injection through a catheter in the right heart or pulmonary trunk is preferable for consistent, precise films and provides the added opportunity to obtain right heart and pulmonary arterial pressure measurements. Rapid sequence studies record the progression of dye through the pulmonary circulation and accurately outline anatomic abnormalities in the pulmonary arteries. An abrupt termination of a column of contrast media marks the site of large vessel obstruction, and non-occlusive emboli are demonstrated by intraluminal filling defects. Regional abnormalities indicating pulmonary embolism include avascular areas, regions with small pulmonary arteries of reduced caliber, and areas of decreased blood flow demonstrated by dye retention in arterioles. Pulmonary arteriography is less sensitive but in some instances more specific than lung scanning as a diagnostic procedure. Since pulmonary arteriography is slightly more hazardous than scanning, its use is preferably restricted to patients with equivocal lung scans in whom an objective diagnosis is mandatory.

Management

In addition to general supportive care, anticoagulation is basic to management of all patients with pulmonary embolism[27]. Heparin has rapid, controllable action, and is the preferable agent for initial anticoagulation in thrombophlebitis and pulmonary embolism. A clotting time of at least twice the normal value should be maintained at all times. Heparin anticoagulation is begun by intravenous injections repeated every four hours and usually requires 40,000 units of heparin a day[28]. After several days, subcutaneous or intramuscular heparin administration provides adequate protection while oral coumadin anticoagulation is being established. Prophylactic or long-term anticoagulation is best achieved by oral administration of a coumadin derivative to reduce the prothrombin time to 25 percent of normal. The optimal period to continue anticoagulation after pulmonary embolism is uncertain, but therapy should not be discontinued before the patient is fully ambulant. The rationale for anticoagulation of patients with pulmonary embolism is the prevention of both *in situ* thrombosis in occluded pulmonary arteries and further thrombosis at the original sites in the systemic veins. In addition to its anticoagulative effects, heparin may be of value in relief of bronchiolar constriction. Anticoagulation greatly reduces the mortality of pulmonary embolism, and reports of fatal embolism in patients adequately treated with heparin are uncommon[27 29]. Moreover, controlled studies have demonstrated a marked reduction of thromboembolism in high risk patients receiving prophylactic anticoagulation[30]. Disorders which predispose to bleeding contraindicate anticoagulation, and all patients who receive therapy should be observed cautiously for hemorrhage. However, less than one percent of properly selected patients develop significant hemorrhagic complications after anticoagulation. The effectiveness of anticoagulation in prevention and treatment of pulmonary embolism justifies this amount of risk.

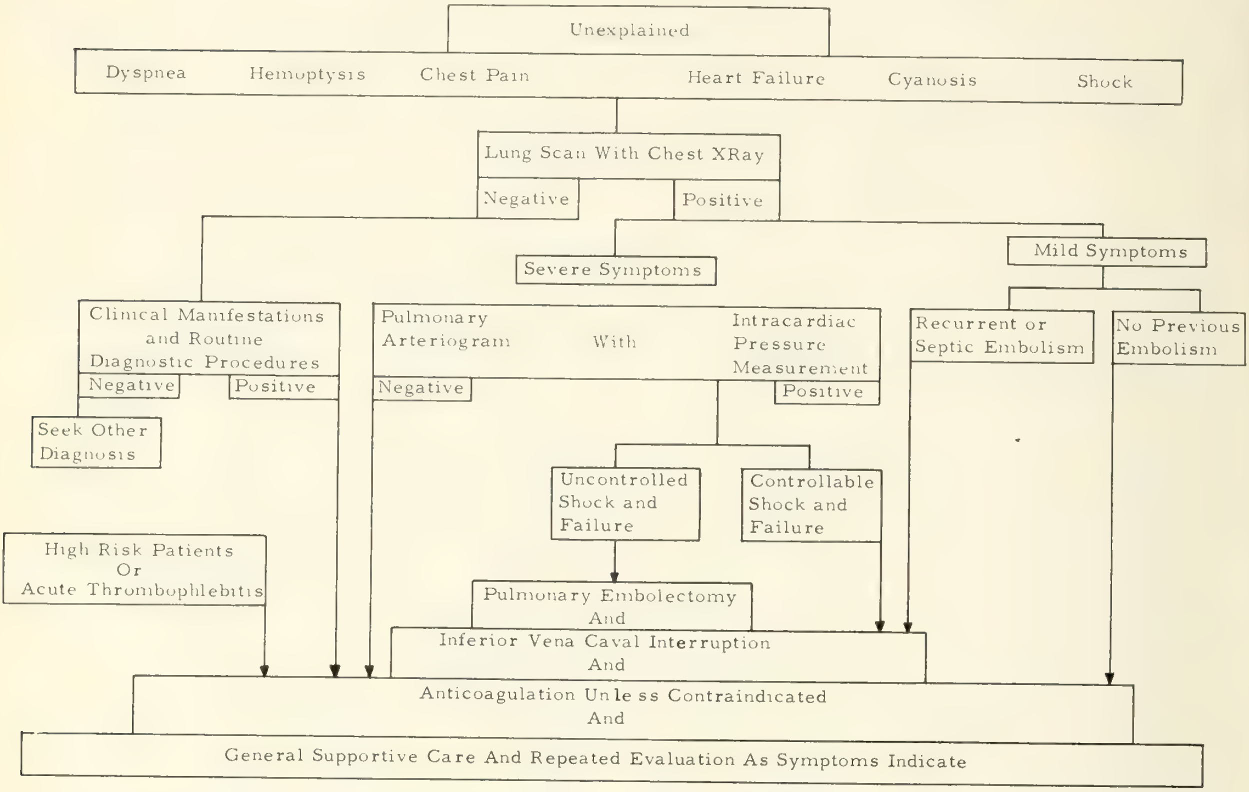
Since the majority of pulmonary emboli arise in the veins of the lower limbs and pelvis, interruption of the inferior vena cava is advocated by many as additive to the protection. Interruption of the inferior vena cava also offers an alternate method of treatment for patients in whom anticoagulation is contraindicated. It has been documented clearly that inferior vena caval ligation frequently causes venous stasis in the legs, and a variety of surgical procedures dividing the vena cava into small channels have been devised in an effort to circumvent this complication. The surgical procedure of choice for interruption of the inferior vena cava in most patients remains controversial. Complete ligation, plication with residual small channels, or the application of partially occluding clips have each been endorsed. The prime indications for caval interruption include those patients with repeated showers of small emboli causing cor pulmonale or those with septic emboli. Vena caval interruption prevents massive pulmonary embolism from the lower body, but recent data has shown that embolism may recur in up to 20 percent of patients after inferior vena caval ligation either through collateral vessels or from venous sources above the site of interruption[31]. The operative mortality of inferior vena caval interruption is two to five percent, and as many as half the patients develop some degree of postoperative venous stasis in the legs. In each patient the potential benefit must be carefully weighed against the hazards of vena caval interruption. It should be emphasized that while this procedure is not a difficult one, it has the potential for producing significant postoperative morbidity in many patients. Clearly, it should be reserved for those patients in whom it is considered mandatory. Moreover, a *definite* diagnosis of pulmonary embolism, either by scan or arteriogram, should be established prior to operation.

Direct removal of emboli from pulmonary arteries is a surgical technic introduced by Trendelenburg in 1908. Although originally performed by simple interruption of the circulation, today total cardiopulmonary bypass is preferred. Median sternotomy is followed by opening of the pulmonary arterial trunk with extraction of the emboli by forceps, suction and lung massage. After completion it may be elected to interrupt the inferior vena cava. Anticoagulation is maintained in the postoperative period[32]. Although dramatic improvement follows pulmonary embolectomy in some patients, many patients treated with anticoagulation alone also survive massive pulmonary embolism and regain blood flow in occluded pulmonary arteries. The very high mortality in patients with disorders other than pulmonary embolism who are subjected to embolectomy emphasizes the necessity for an accurate preoperative diagnosis made by pulmonary arteriogram. An overall operative mortality of 50 percent suggests that pulmonary embolectomy should be reserved for patients who appear unlikely to survive massive pulmonary embolism with anticoagulation therapy alone[33]. In general, the presence of refractory shock is the most justifiable indication for pulmonary embolectomy.

Prevention is the most satisfactory treatment of pulmonary embolism. In surgical patients gentleness in operative technic, avoidance of limb compression in anesthetized patients, and early postoperative ambulation decrease the incidence of venous thrombosis. Elevation of the foot of the bed (approximately 15 degress) reduces venous stasis in legs of immobile patients. Patients over the age of 45 who are confined to bed for prolonged periods, especially in the presence of tissue injury, should receive prophylactic anticoagulation. Patients with signs suggestive of thrombophlebitis of the legs should be placed on anticoagulation therapy and observed closely for pulmonary embolism. When preventive measures fail, recognition of the clinical manifestations of pulmonary embolism allows rapid diagnosis with institution of proper therapy. A logical approach to the diagnosis and treatment of pulmo-

Figure I

Diagram of Clinical Management of Patients with Pulmonary Embolism


Unexplained
Dyspnea
Hemoptysis
Chest Pain
Heart Failure
Cyanosis
Shock
Lung Scan With Chest XRay
Negative
Positive
Severe Symptoms
Mild Symptoms
Clinical Manifestations and Routine Diagnostic Procedures
Negative
Positive
Seek Other Diagnosis
Pulmonary Arteriogram With Intracardiac Pressure Measurement
Negative
Positive
Recurrent or Septic Embolism
No Previous Embolism
Uncontrolled Shock and Failure
Controllable Shock and Failure
High Risk Patients Or Acute Thrombophlebitis
Pulmonary Embolectomy And
Inferior Vena Caval Interruption And
Anticoagulation Unless Contraindicated And
General Supportive Care And Repeated Evaluation As Symptoms Indicate

nary embolism is outlined in Figure I. Because most patients with pulmonary embolism have only non-specific symptoms, all unexplained dyspnea, hemoptysis, chest pain, heart failure, cyanosis or shock demand that a lung scan be performed. Massive pulmonary embolism is excluded by a normal lung scan, but small emboli cannot be detected by lung scan. Therefore, if clinical manifestations suggest pulmonary embolism which is not confirmed by lung scan, anticoagulation is indicated. Severity of symptoms determines the management of patients with a lung scan diagnosis of pulmonary embolism. Patients with mild symptoms are treated with anticoagulation alone unless embolism is recurrent or septic, in which case vena caval interruption should be considered. The lung scan is often sufficiently sensitive to detect small emboli not demonstrated on pulmonary arteriogram. Treatment of patients with massive pulmonary embolism with an established diagnosis by pulmonary scan or arteriogram is dictated by the severity of circulatory abnormalities. Pulmonary embolectomy is essential for patients with systemic hypotension and right ventricular failure which cannot be controlled by medical management. Patients with controllable circulatory alterations after massive pulmonary embolism should be maintained with anticoagulation and medical management until a stable general condition permits vena caval interruption. Clinical judgment must temper application of these generalizations to individual patients. Correct diagnosis is essential for proper management of patients with pulmonary embolism. Complete evaluation of patients suspected of having pulmonary embolism by this systematic approach requires only a relatively short time. The hazards of surgical therapy for pulmonary embolism justify this delay even in severely ill patients.

Summary

Pulmonary embolism is a common and often fatal disorder. Massive embolism abruptly increases pulmonary arterial pressure, and severe obstruction causes right heart failure, shock and death. Emboli which are not fatal gradually resolve in the pulmonary circulation. Dyspnea is the most common clinical manifestation in pulmonary embolism, and other signs are frequently inconsistent and often vague. The chest film, electrocardiogram and serum enzyme determinations are helpful although frequently unreliable procedures in establishing an objective diagnosis. Lung scanning is a

safe, sensitive procedure for initial evaluation, and pulmonary arteriography may be necessary in certain patients for confirmation. Anticoagulation therapy is effective in the prevention and treatment of pulmonary embolism. Vena caval interruption or pulmonary embolectomy are beneficial in selected patients with pulmonary embolism. The hazards of these surgical procedures demand that a definite preoperative diagnosis of pulmonary embolism be made. A systematic approach to diagnosis and treatment of pulmonary embolism is presented and recommended.

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Surgical Treatment of Extracranial Cerebral Vascular Occlusive Disease

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Strokes are a major complication of cerebral atherosclerosis. Precise statistics regarding incidence of cerebrovascular disease is lacking but in a gross way the importance of the problem is attested by the fact that 12 per cent of all deaths in the United States are attributed to these causes ranking them in third place behind diseases of the heart and cancer.[3] The number of persons living with significant disability due to strokes has been variously estimated at between 500,000 to 2,000,000. An estimated one-third of cerebral vascular accidents result from occlusive lesions in the cervical portions of the carotid and vertebral arteries in a location which permits definitive surgical treatment with restoration of normal cerebral circulation. A heavy responsibility is thus placed on physicians who see patients with cerebral symptoms, since recognition of the early signs and symptoms may prevent a major cerebral catastrophe. Arteriography must be recommended early and operation performed before a stenotic lesion progresses to complete occlusion and irreversible brain damage occurs.

Anatomy and Pathology of Extracranial Vascular Occlusive Disease

Blood supply to the brain is derived from the internal carotid arteries and the vertebral arteries. The internal carotids branch intracranially into the anterior and middle cerebral arteries supplying the cerebral hemispheres. The ophthalmic artery, which supplies the retina and ocular structures, is the first intracranial branch of the internal carotid artery.

The vertebral arteries join at the brain stem to form the basilar artery which divides into the posterior cerebral arteries. The posterior communicating arteries connect the posterior cerebral arteries to the carotid systems anteriorly and these vessels along with the anterior communicating artery (between the two anterior cerebral arteries) complete the circle of Willis. The vertebrobasilar system supplies the posterior fossa structures: the pons, medulla and cerebellum. Nuclei of cranial nerves are supplied largely by branches of the basilar artery.

Most of the surgically correctable extracranial lesions that produce transient ischemic attacks are located at the point where the common carotid artery bifiurcates into internal and external branches and at the origin of the vertebral artery from the subclavian artery. These lesions are atherosclerotic plaques that produce obstruction to blood flow. Most such lesions are localized to short segments involving 2 or 3 centimeters of vessel, but some are more extensive. In general the degree of interference with circulation is related to diameter of lumen and length of plaque. The vessel distal to an atherosclerotic plaque is usually free of disease.

Atherosclerotic plaques contain lipids, fibrin, calcium, and other debris. Occasionally these plaques rupture or ulcerate discharging particulate matter into the cerebral circulation. This process may account for the presence of transient neurologic symptoms in the patient with only mild to moderate mechanical obstruction demonstrated on arteriogram. Elongation and tortuosity of the internal carotid artery may result in kinking of the vessel with intermittent obstruction. Elongation may be extreme and result in the formation of a complete loop. Flexion of the neck may produce sudden vascular occlusion with onset of symptoms.

The final event in the evolution of atherosclerotic stenosis of a vessel is complete occlusion with possible cerebral infarction. If collateral circulation is adequate distal to a completely occluded carotid or vertebral artery, cerebral infarction may be delayed or may not occur. Operation performed within a few hours of complete cartoid occlusion may be successful in restoring patency but revascularization in such cases may result in death due to sec-

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From the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine and the Texas Heart Institute of St. Luke's and Texas Children's Hospitals, Houston, Texas.

ondary cerebral edema or hemorrhage into an infarct. Restoration of flow through a chronically occluded internal carotid artery is usually not possible because the occlusive process culminates in fibrosis and extends cephalad to the first intracranial branch, the ophthalmic artery. Thus operation is seldom advisable in chronically totally occluded carotid arteries.

The arteritis which produces the aortic arch syndrome begins as an inflammatory lesion and heals by scarring and vascular occlusion. The affected artery becomes a fibrous cord and direct repair is usually not possible. Bypass or excision and graft replacement is necessary.

Diagnosis

Extracranial vascular occlusive lesions are usually atherosclerotic in nature and tend to occur in patients more than 40 years of age. An unusual form of inflammatory arteritis tends to occur near the origins of the brachiocephalic vessels from the aortic arch in adolescents and young adults. The "aortic arch syndrome" typically occurs in young women in the second, third, and fourth decades of life and is prevalent in the Far East where it is known as Takayashu's disease.

Symptoms and findings exhibited by patients with cerebral vascular insufficiency vary according to whether there is predominant involvement of the carotid or the vertebrobasilar system. Manifestations of the carotid syndrome include: contralateral hemiparesis or hemiplegia, dyphasia or aphasia (if dominant hemisphere is involved), and ipsilateral monocular blindness (due to reduction in flow through the ophthalmic artery). Manifestations of the vertebrobasilar syndrome include: diplopia, facial weakness, cerebellar signs (vertigo, loss of equilibrium, ataxia, etc.), blindness, syncope, other disturbances of consciousness and motor and sensory tract signs.

Patients with symptoms and signs suggesting the carotid syndrome usually fall in one of three categories.

1. *Transient Ischemic Attacks:* Symptoms appear suddenly, last for several minutes to several hours and clear completely.

2. *Progressive Stroke:* Manifestations persist and progress over a period of hours or days. Symptoms and signs may wax and wane, but the overall pattern may be one of progressive deterioration.

3. *Completed Stroke:* Onset of symptoms and signs is sudden but may occur over a period of several minutes. The typical picture is one of sudden onset of hemiplegia and aphasia due to decreased blood flow to dominant hemisphere.

Physical findings depend on whether a carotid or a vertebrobasilar syndrome is present and on the stage of ischemia in which the patient is seen. Physical findings may vary from none in a patient with transient ischemic attacks to hemiplegia and aphasia in a patient with a completed carotid stroke.

Especially important in physical examination of the patient is auscultation of the neck for vascular bruits as a sign of partial arterial obstruction. The diaphragm of the stethoscope should be placed over the carotid bifurcation near the angle of the jaw and over the subclavian artery just above the clavicle at the point of origin of the vertebral artery. Significant obstructing or ulcerating lesions may be present in the absence of bruits.

Inequality of pulses and blood pressures in the arms indicates stenosis or occlusion of a subclavian or innominate artery. A markedly elevated blood pressure may indicate that cerebral symptoms are a result of hypertensive encephalopathy or intracerebral hemorrhage.

Routine laboratory studies should include a complete blood count, serology, urinalysis, blood urea nitrogen, blood sugar, and serum electrolytes. Metabolic conditions such as diabetes and uremia may thus be ruled out as a cause of cerebral symptoms. Roentgenograms of the chest and skull are indicated. Electroencephalograms are often helpful, particularly in revealing patterns of epilepsy and brain tumor. Echoencephalograms and radioactive brain scans are useful adjuncts in diagnosis.

Cerebral arteriography is the most important maneuver in the study of patients with cerebral symptoms. This test identifies patients with brain tumors and permits recognition of those with cerebrovascular insufficiency who have operable extracranial occlusive lesions. All patients with symptoms or signs suggesting cerebrovascular insufficiency should have cerebral arteriograms.

Technic of Arteriography

We prefer to perform cerebral arteriograms on patients under moderate sedation using local analgesia. The patient is placed in the supine position and 18 gauge Cournand needles are inserted into the common carotid arteries at the anterior borders of the sternomastoid muscles 4 cm. above the clavicles. The needles are carefully threaded upward. Eight milliliters of Conray® contrast medium are injected at moderate speed. Films including the head and neck are exposed in the lateral and anteroposterior positions for each carotid artery (Fig. 1).

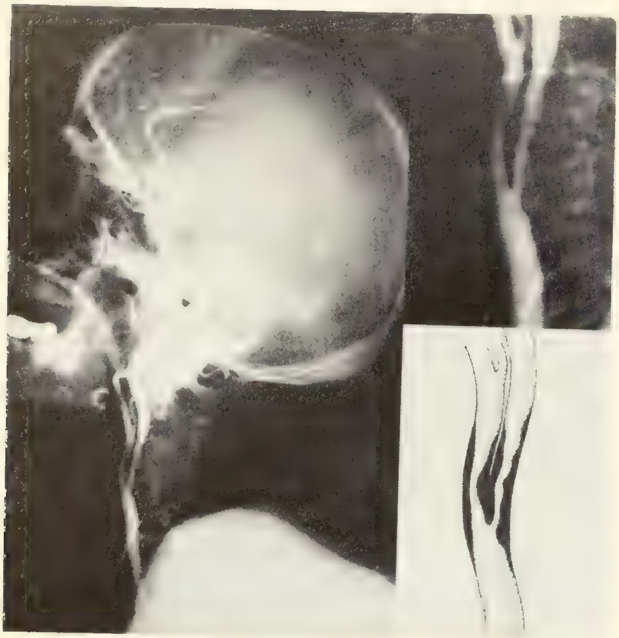

Figure 1
Left carotid arteriogram in a 73 year old woman with loud carotid bruits. Note long area of stenosis at bifurcation seen better in close-up view. The internal carotid artery is posterior. Drawing illustrates extent of lesion.

Vertebral arteries are visualized by introducing 17 gauge Cournand needles into the subclavian arteries beneath the clavicles as the artery passes over the first rib. Forceful manual injection of 20 milliliters of Conray® produces retrograde filling of the subclavian artery and its branches. The vertebral artery is visualized throughout its cervical and intracranial course (Fig. 2). Stenosis of a vertebral artery is a relatively uncommon cause of cerebrovascular insufficiency. We, therefore, do not believe it mandatory to perform bilateral subclavian-vertebral arteriograms in all patients undergoing carotid arteriograms. Whereas we believe that all patients with symptoms suggesting cerebrovascular insufficiency should have carotid arteriograms, we study the subclavian-vertebral circulation only in patients with certain indications. These include: brainstem or cerebellar signs, supraclavicular bruit, and unequal pulse or blood pressure in the arms. The presence of dizziness as a sole symptom might be an indication for subclavian-vertebral arteriograms, but the majority of patients with dizziness and carotid stenosis obtain relief by carotid endarterectomy even if a vertebral lesion is present.

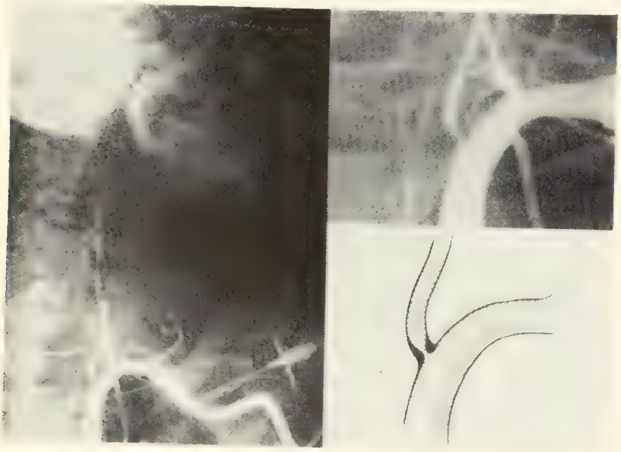

Figure 2
Left subclavian-vertebral arteriogram in a 62 year old man Marked stenosis of proximal vertebral is readily apparent especially in close-up view. Drawing illustrates nature of lesion.

Vertebrobasilar insufficiency rarely follows stenosis or occlusion of only one vertebral artery, since one vessel is normally sufficient to supply the basilar system. Patients with vertebrobasilar symptoms on the basis of vascular insufficiency usually have stenosis or occlusion of both vertebral areteries or stenosis of one and occlusion of the other.

"Subclavian Steal Syndrome"

A special form of vertebrobasilar insufficiency occurs in the "subclavian steal" syndrome. These patients have proximal stenosis or occlusion of a subclavian artery. Pressure in the distal vessel including that part giving rise to the vertebral artery is reduced. A discrepancy in the pulse and blood pressure in the two arms is, therefore, an important diagnostic finding.

On exercise of the affected arm the extra blood demanded by its muscles enters the distal subclavian artery by retrograde flow from the vertebral artery, thus siphoning or "stealing" blood away from the basilar artery and circle of Willis. This produces dizziness and other symptoms of vertebrobasilar insufficiency. Claudication or other symptoms of ischemia may be present in the involved arm or hand. Arteriography demonstrates the subclavian stenosis and retrograde flow through the vertebral artery (Fig. 3).

Surgical removal or bypass of the obstructing subclavian lesion eliminates the pressure differential, stops the "steal" phenomenon, and relieves symptoms.

Surgical Treatment

Treatment of extracranial occlusive disease producing cerebral vascular insufficiency depends on the stage of evolution of disease in which the patient is first seen.

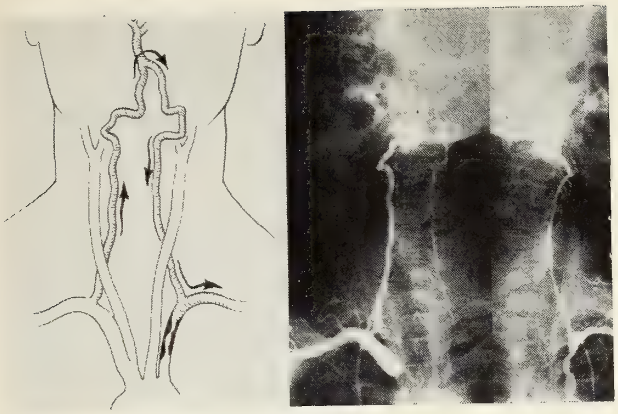

Figure 3

Bilateral subclavian-vertebral arteriogram showing subclavian steal phenomenon. On left is drawing of vertebral circulation with arrows indicating flow up right vertebral and retrograde down left vertebral into left subclavian artery. Note proximal left subclavian stenosis. In center is an early exposure with contrast material going up right vertebral and down left vertebral. Later exposure showed contrast material entering left subclavian artery. On right is film exposed on injection of left subclavian artery delineating proximal stenosis.

1. *Completed Stroke:* Treatment of a patient with a completed stroke is primarily medical and supportive. Emergency operation is seldom successful and may be fatal. Arteriograms may be done after the patient's condition has stabilized to determine if an extracranial lesion is present. If the patient has a hemiplegia and a complete carotid occlusion is found on the side opposite the paralysis, little can be gained by operation. If a stenotic lesion is found on either side in the hemiplegic patient, operation could be justified on the basis of prophylaxis against subsequent strokes. There is no assurance that pre-existing paralysis will be improved.

2. *Progressive Stroke:* Management of a patient with a progressive stroke must be individualized. In general arteriograms should be done soon unless the patient is improving. If the patient is improving arteriograms should be delayed until neurologic manifestations have stabilized. If an extracranial lesion is identified, it should be repaired.

3. *Transient Ischemic Attack:* Best results in the treatment of cerebrovascular insufficiency are obtained in patients with transient ischemic attacks due to localized extracranial stenotic lesions of the carotid and vertebral arteries. Removal of obstructing plaques by endarterectomy followed by widening of the operative area through application of a Dacron® patch in the arteriotomy restores normal pulsatile flow through the previously obstructed area (Figs. 4 and 5). Tortuous, "looped" or kinked segments of internal carotid artery are excised or the proximal portion of the internal carotid can be implanted at a more proximal site on the common carotid eliminating redundancy. Surgical treatment of the aortic arch syndrome or subclavian "steal" phenomenon includes use of bypass Dacron® tube grafts attached proximally to a normally pulsating vessel and distally to a disease free artery beyond the obstruction.

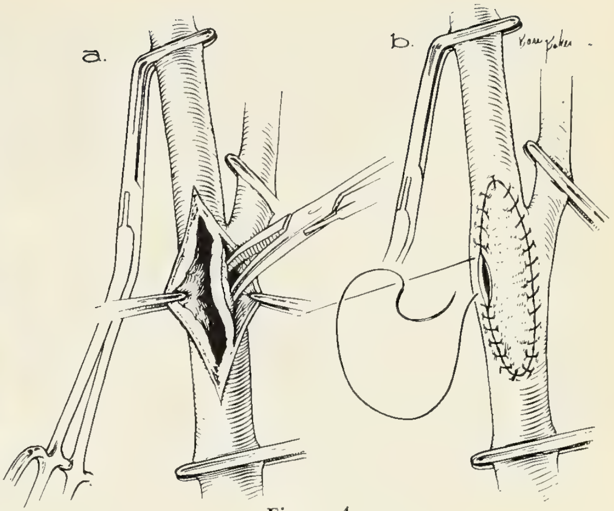

Figure 4

Drawings illustrating carotid endarterectomy. a. Vascular clamps placed and plaque peeled out by endarterectomy. b. Operative area widened by suturing Dacron patch into incision. No shunt used (see text).

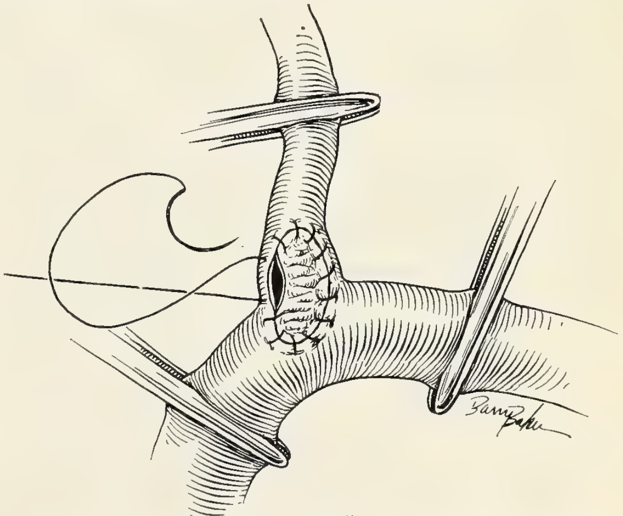

Figure 5

Drawing of vertebral operation. Obstructing plaque has been removed by endarterectomy. Dacron patch sutured into arteriotomy widening the area.

Operations for extracranial vascular occlusive lesions are performed under general anesthesia for maximal cerebral protection. The patient is allowed to accumulate carbon dioxide so that cerebral vasodilatation will maximize cerebral blood flow. Hypertension usually accompanies the resultant hypercarbia and further enhances cerebral circulation. Cyclopropane with high oxygen content is used for anesthesia. Under these circumstances an internal carotid shunt is not necessary.[1 4]

Our experience with surgical treatment of extracranial cerebral vascular occlusive disease now extends to over 2500 operations in 2000 patients. The most encouraging results are obtained in patients with transient ischemic attacks.[2] In this group the mortality rate has been only three per cent in spite of advanced age and involvement of other organ systems by atherosclerosis. Eighty-nine per cent of these patients are relieved of their symptoms or obtain significant improvement after relief of extracranial vascular obstruction.

Summary

Intermittent symptoms of unilateral weakness or numbness, speech difficulty, or dizziness are frequently the result of cerebrovascular insufficiency. These ischemic episodes are often caused by stenosis or occlusion of major vessels in the neck: the carotid and vertebral arteries. A vascular bruit is an important diagnostic sign when heard near the angle of the jaw or just above the clavicle. Cerebral arteriography is mandatory in all such patients to demonstrate the exact site and precise nature of the lesion.

Surgical removal of the obstructing process should be carried out and usually results in complete relief of symptoms with low morbidity and mortality. To avoid permanent paralysis and death, surgery must be performed before complete vascular occlusion occurs.

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The shock of retirement is not that you stop doing something, but that you do not start doing something else.

Most patients are not afraid of death but are reluctant to die.

It is notorious that the desire to live increases as life itself shortens.

Hamon y Cajal

Surgery in the Treatment of Coronary Artery Disease

Donald B. Effler, M.D.

The time-honored methods of diagnosis and treatment for ischemic heart disease have changed little in recent years. If one considers coronary arterial disease as analogous to other forms of vascular disease it would seem that a great deal more could be done to meet the needs of patients who suffer from this all too common ailment. Arteriography, which is used extensively to evaluate patients with aortic, peripheral, renal, carotid, or intracranial arterial disease is not utilized by most cardiologists who are responsible for diagnostic evaluation of the coronary patient.

In 1958, F. Mason Sones, Jr., M.D., of the Cleveland Clinic introduced selective coronary arteriography[3]. This invaluable procedure has a tremendous potential for improving the clinician's understanding of coronary artery disease. Nevertheless, 10 years after its inception, coronary arteriography is employed sparingly, if at all, in many medical centers that offer specialty training in cardiology.

The Cleveland Clinic experience now exceeds 11,000 studies performed by Doctor Sones and his co-workers. Technical refinements have made coronary arteriography a safe, practical procedure, which establishes the presence or absence of coronary artery disease. When diagnosis of coronary artery disease is established, the technic helps the physician to assess the specific needs of his patient and to determine an appropriate form of treatment.

Surgical Treatment

Operations intended to revascularize ischemic myocardium have been undertaken for several decades. It will serve no purpose to list the variety of operative ventures that comprise the early era of surgery for coronary artery disease. That this era began with enthusiasm and ended in disappointment is well-known medical history. However, a new era of coronary artery surgery was initiated by selective coronary arteriography. With precise diagnosis the need for revascularization in the individual patient could be determined. Postoperatively this technic offers a realistic method of evaluating the success or the failure of the surgical treatment. The importance of Sones's contribution can be stated simply—coronary artery surgery begins and ends with selective coronary arteriography.

Selection of patients. The majority of patients under consideration for revascularization procedures have had a trial of medical therapy. A significant number have already sustained one or more infarctions. Dissatisfaction on the part of the patient and his physician prompts consideration for surgical treatment. This treatment, properly applied, can either increase blood flow to the ischemic myocardium or imrove function of the damaged left ventricle.

Revascularization surgery is appropriate for the patient who suffers from a myocardial perfusion deficit that is not relieved by conventional medical therapy[1]. Such a patient will have angina pectoris and may have already sustained myocardial damage due to infarction or chronic ischemia. To cardiac surgeons, angina pectoris is comparable to claudication, and implies a stressful period with anaerobic metabolism when myocardium is perfused inadequately. This status is arteriographically evident by demonstration of severe occlusion in a proximal coronary artery that supplies the left ventricle. Additional evidence is present when collateral blood vessels are seen supplying the area in question. Therefore, the patient who has angina pectoris and arteriographic evidence of myocardial perfusion deficit, is given consideration for surgical treatment of his definitive coronary arterial disease.

Surgical approaches. Rehabilitation of the patient who suffers from ischemic heart disease may be provided by operations that: (1) improve left ventricular function[3], (2) remove coronary arterial obstruction[2], or (3) offer a new source of myocardial blood supply[4].

(1) Left ventricular reconstruction. Patients who survive major myocardial infarctions may be in-

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valided by ventricular aneurysms, full-thickness ventricular scars, or incompetent mitral valves (ruptured chordae tendineae or infarcted papillary muscle). Such patients have presenting signs of enlarged hearts, and histories of reduced exercise tolerance, chronic or recurrent congestive manifestations, and paroxysmal arrhythmias. Ventriculography, which is used along with selective coronary arteriography, demonstrates impaired contraction or paradoxic motion of the involved wall of the left ventricle. The patient who is handicapped by ventricular aneurysm, or a large, full-thickness scar on the anterior wall of the left ventricle, may benefit by surgical excision of the damaged tissue. This rehabilitative procedure is accomplished with extracorporeal circulation which permits total circulatory bypass of the damaged heart. If the mitral valve is rendered incompetent by ischemic changes in the chordae tendineae or papillary muscle, plastic repair or reconstruction of the valve is indicated—not infrequently this will be an accompaniment of ventricular aneurysmectomy. Whenever possible, reconstructive surgery of this type should be deferred until six months or more have elapsed since the nearly catastrophic infarction. Under ordinary conditions, the hospital mortality rate in regard to this form of surgical treatment of acquired heart disease is less than 10 percent.

(2) Direct coronary artery surgery. Arteriography proves that most patients with coronary arterial disease have a diffuse pattern of their pathologic condition; nevertheless, a significant number will have a sharply localized segmental occlusion of a major coronary vessel. Surgical relief of a segmental obstruction may be accomplished by use of a pericardial patch graft, or by total excision and replacement of the diseased segment with an interposed saphenous vein graft.

The greatest application for direct coronary arterial surgery is for segmental occlusion that occurs in a dominant right coronary artery. The extensive experience of Sones and his colleagues indicates that the right coronary artery perfuses the posterior aspect of the left ventricle, intraventricular septum, and papillary muscles in about 75 percent of patients who have been studied. The dominant right coronary artery by its anatomic position and other features lends itself well to direct surgical treatment. In contrast, the left coronary artery has certain features that make it much less attractive to the surgeon, and direct operations upon this vessel carry an almost forbidding element of risk.

At this writing, more than 200 patients have been operated upon for direct coronary artery surgery, at the Cleveland Clinic Hospital. The first 130 patients underwent endarterotomy with pericardial patchgraft reconstruction—some excellent long-term results have been obtained, but this surgical technic has distinct limitations. At the present time the Cleveland Clinic team favors direct excision of the diseased arterial segment and replacement by an interposed saphenous vein graft. This technic is, in some ways, far simpler than the original patchgraft procedures, and it promises to broaden the scope of direct coronary artery surgery in the immediate future.

(3) Mammary artery implant procedures. Revascularization by implantation of the internal mammary artery was suggested by Vineberg in 1946. Vineberg's hypothesis is based upon the observation that collateral blood vessels from a healthy source will grow when a functional demand of blood exists, providing that the host tissue has not been damaged beyond repair. From a practical standpoint, an internal mammary artery procedure will succeed when a perfusion deficit exists in the left ventricular myocardium.

The Vineberg procedure was first undertaken at the Cleveland Clinic in 1962, after Sones had evaluated a small, but impressive group of patients who had been operated upon in Canada by Vineberg of Montreal and Bigelow of Toronto—each of these patients was demonstrated to have severe coronary atherosclerosis, and opacification of the internal mammary artery implant proved that revascularization had been accomplished. Considerably modified, the Vineberg procedure has been utilized by the Cleveland Clinic team in more than 1,300 operations. Increasing experience has shown that the potential of internal mammary artery implant procedures is far greater than has been anticipated. Perfusion deficits occurring in any area of left ventricular myocardium may be corrected by a strategically placed internal mammary artery implant. In patients with unusually severe disease, the perfusion deficit may be total in the left ventricle, and in these patients, a double implant that utilizes both the right and the left internal mammary arteries is indicated.

The most common site of single coronary artery occlusion occurs in the anterior descending branch of the left coronary artery. This is particularly true in younger male patients, for this reason it has become common practice to implant the right internal mammary artery into the anterior wall of the left ventricle, by means of a sternal split incision. In this way the left internal mammary artery is preserved, and may be used later if progress of the disease creates perfusion deficit in the lateral or diaphragmatic aspect of the left ventricle.

An additional potential use for mammary artery implant procedures is seen in patients who require a combination of surgical procedures. As an example: an operation for direct removal of a right coronary segmental obstruction or a ventricular aneurysmectomy may be augmented by a complementary implant procedure on the lateral and diaphragmatic aspect of the ventricle. The variety of applications of these various surgical procedures has been recognized from the accumulation of evidence provided with postoperative coronary and mammary arteriography.

Comment

Many physicians—internists and surgeons alike—remain skeptical of the claims made for current revascularization surgery. The majority of critics have not, or will not, expose themselves to selective coronary arteriography as it is applied in the selection of patients for revascularization surgery and as a means of reevaluating those who have survived such procedures. Others will argue that the introduction of a new blood supply does not alter the basic problem, or that the relief of angina by surgical means is an unreliable means of assessing value. The fact remains, though, that the enthusiasm associated with this new era of coronary artery surgery is steadily increasing, not only at the Cleveland Clinic, but in many centers throughout this and other countries. The time for stubborn skepticism has long since passed, and the need for greater participation by those responsible for the treatment of patients with coronary artery disease is apparent.

Summary and Conclusion

Selective coronary arteriography has introduced a new era in the surgical treatment of coronary arterial disease. Since 1962, three basic surgical approaches have been utilized to reconstruct the damaged left ventricle or to provide increased blood flow to ischemic ventricular myocardium. Better understanding of revascularization potential has improved the selection of patients for this type of surgical treatment, and has increased the yield of desired results. Continued refinements in surgical technic are reducing the risk of operation and at the same time extending the application of this type of procedure to the realm of the community hospital.

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THE PRESIDENT'S PAGE

This is the season when we give thanks for the blessings we have. Surely, in this country we have more to be thankful for than any place on earth. Too often we allow ourselves to be occupied by the petty annoyances of small inconveniences. It is a pity that humans always tend to make small matters so important.

How wonderful it is to be a part of a system of healing which knows no equal in all the world. We can all point with pride to the accomplishments medicine has made and is still making. Certainly each one does his part to make this possible.

We must be thankful that there are men who are willing to risk their lives in a distant land for the sake of their country. All this with scant hope of recognition from what must seem to them to be an ungrateful world. Perhaps we should do more to make our servicemen aware of our thanks. Certainly, life would be much less sweet under another form of government.

The members of the Connecticut State Medical Society have a great deal to give thanks for. Members of the Council, those men who meet for hours on end each month carrying on the complicated business of the society, deserve the heartfelt thanks of all. The Council is surely made up of dedicated men who never seem to complain about added burdens. We could not keep medicine's house in order without them. It is a large task they perform.

Dr. William Richards, Mrs. Josephine Lindquist, Mr. Peter Villano and their staff are a marvel. They are absolutely dedicated to the doctors of Connecticut. Without them life would be much more difficult for us all.

While we are being thankful, let us not forget Connecticut Medicine and its devoted editor. All of us take pride in the excellence of our state journal.

It is a pretty good Thanksgiving all around.

NORMAN H. GARDNER, *President*

FROM THE GENERAL MANAGER'S OFFICE

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CALL

SEMI-ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1968 Semi-Annual Meeting of the House of Delegates will be held at the Stratford Motor Inn, Stratford, commencing at 2:00 o'clock in the afternoon of Wednesday, December 11.

Norman H. Gardner, President
Kenneth F. Brandon, Speaker of the House
Frederick C. Weber, Jr., Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12 Par. 3 of the By-laws provide that:

> *All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.*

SUMMARY OF ACTIONS
COUNCIL MEETING
Wednesday, September 25, 1968

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Caplan, Grendon, Abbot, Fabro, Bradley, Rogol, Farrell, Egan, Petrie, Spitz, Purnell, Shepard, Nemoitin, Johnson, Friedberg, McDonald, Granoff, Wilson and Palomba.

Also present were: Mrs. Lindquist, Mr. Villano, Dr. Redlich, Dr. Patterson, Dr. Hess and Dr. Richards.

Absent were: Drs. Weber, Jr., Brandon, Cramer, J. Grant, R. Grant, Pelz and Roch.

II. Routine Business

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Bernard S. Brody, New Haven (NHCMA)—1969
Pasquale Lombardi, Waterbury (NHCMA)—1968
Robert A. Northrop, Norwalk (FCMA)—1969

CSMS Dues Exemptions

It was VOTED to exempt from payment of CSMS membership dues the following Active Members, for the reasons and periods indicated:

Frederick Burkle, New Haven (NHCMA)—1968—Military duty
Robert Dutton, Branford (NHCMA)—1968—Military duty
Edward Jacobs, New Haven (NHCMA)—1968—Military duty

Date of Next Meeting

Since at 7:00 P.M. not more than half the items on the agenda had been taken up, it was VOTED to recess the meeting of September 25, 1968 until 2:00 P.M. on Thursday, October 10, 1968.

III. Old, New and Special Business

Report—Ad Hoc Study Committee on "Tri-Sate Plan"

It was VOTED to receive as information a report filed by this Ad Hoc Committee on its study of the structure, objectives and costs of the State-sponsored "Regional Health Resources and Services Information System for Coordinating Planning and Management for Connecticut, Massachusetts and Rhode Island". Since it is understood that the grant request for this project is still under study by the U.S. Public Health Service, it was further VOTED to request the Ad Hoc Committee to keep the Council informed of developments relating to this "Tri-State Plan" for gathering information on health resources and services. It was further

VOTED to request the Ad Hoc Committee to prepare a critical analysis of the "Tri-State Plan" section by section, and report on same to the Council with any recommendations indicated.

Resolution on Smoking in Hospitals

It was VOTED to remove from the table and discuss further a resolution on this subject submitted by Marcel Thau, Hartford, in July of this year. An additional plea for Council adoption of a resolution on smoking in hospitals was also received from Joseph J. Kristan, Rockville, and was considered in the ensuing discussion. Ultimately, it was VOTED to adopt the following:

Resolution
Subject: Smoking in Hospitals

WHEREAS: Cigarette smoking constitutes a serious hazard to health in general; and

WHEREAS: Smoking by visitors in hospitals is often disturbing and perhaps deleterious to some patients; and

WHEREAS: Smoking by hospitalized patients increases the hazard of fire; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society encourage the elimination of the sale of cigarettes on hospital premises; and be it further

RESOLVED: That the Council urge restriction of smoking by patients, personnel and, particularly, by visitors in all Connecticut hospitals; and be it further

RESOLVED: That copies of these resolves be sent to the chiefs of medical staff of all Connecticut hospitals with a request that this subject be discussed at an early meeting of their respective staffs, and that a copy also be sent to the headquarters office of the Connecticut Hospital Association.

Report—Committee on Third Party Payments

Actions were taken on recommendations contained in a report filed by the Committee as follows:

(a) *On Comprehensive Health Insurance Coverage*: It was VOTED that the Council encourage, in principle, reported efforts of the (national) Health Insurance Council to develop a program of comprehensive health insurance coverage; i.e., one which would provide for payment of benefits of the proper type to the various providers of services (physicians, hospitals, laboratories, extended care facilities, etc.), whether services are rendered on an inpatient or outpatient basis. This action was taken in response to the complaint of an NHCMA member that, all too often, patients had to be admitted to the hospital needlessly so as to qualify for benefits for services that could have been rendered on an outpatient basis.

(b) *Updating the CSMS Relative Value Schedule*: It was VOTED to approve the Committee's proposal (and budget for same) to hold a symposium on relative values and the CSMS Relative Value Schedule to orient representatives of CSMS Sections and allied groups as to the rationale for using an RVS in conjunction with the "usual and customary charge" method of payment for physicians' services, and, subsequently, by mail and/or in person, to encourage the participating Sections and groups to submit recommendations for changes in nomenclature, unit values assigned to services, addition of unlisted procedures, etc. Using this approach, the Committee hopes to be able to move forward with the task of "updating" the official CSMS Relative Value Schedule, as requested to by the Council. It was further VOTED to request the Committee to consider the possibility of preparing a (physical) exhibit on relative values for demonstration at the 1969 Annual Meeting of the Society.

Report—Committee on Allied Medical Services

(a) *Training Program for I.V. Technicians*: The Committee reported having held joint discussions with representatives of allied medical services on a proposal to train technicians to administer intravenous therapy to patients in hospitals, the scope of such therapy by these technicians to be limited to certain non-hazardous solutions. The training program is being advanced by Dr. Ronald S. Beckett of the Hartford Hospital. There being a consensus of opinion that not enough was known about the details of this training program to make a considered judgment, it was VOTED to invite Dr. Beckett to join the Council at the next meeting to explain and elaborate on his proposal.

(b) *Nurses' Recognition Day*: At the instigation of the AMA Committee on Nursing, the Committee presented a format for the possible participation of the Society in a "Day" which would give public and professional recognition to the great contributions made by nurses to the care of patients and to the health of the people. In brief, the day would be planned to fall in

"Health Careers Week", October 20-27, 1968, would be proclaimed by the Governor and the Mayors of communities throughout the State, and would involve the Society in several public relations activities (possibly including a TV program) as its part in giving nurses their well-earned recognition. It was VOTED to approve this program, as outlined, and to request the Committee, in cooperation with the PR Director, to implement it.

It was further VOTED to adopt the following resolution:

BE IT RESOLVED: That the Council of CSMS, on behalf of the 3800 physician members of the Society, reaffirm the high esteem in which the profession of nursing is held by doctors of medicine and pay tribute to the nurse as a valued partner of the practicing physician in pursuing their common goal of maintaining a relationship of personal responsibility and personal service to patients.

(c) Having been apprised that, on a voluntary basis at local level, the Connecticut Nurses Association is offering to represent groups of nurses for collective bargaining purposes as part of a "Nurses' Economic Program", and that the National League for Nursing is proposing a selective classification of nurses that would change their present status, designations and functions, the Council VOTED to adopt a resolution as follows:

WHEREAS: The National League for Nursing is reported to have proposed a new classification for nurses which would: (1) label as "professionals" those with academic degrees, (2) label as "technical" those with hospital school diplomas, and (3) label as "vocational" all practical nurses and nurses' aides; and

WHEREAS: The local and national shortage of nurses for patient care may be aggravated by such classification; and

WHEREAS: The Connecticut Nurses' Association is reported to maintain on its payroll two or more persons who promote and help to organize "locals" of the CNA Economic Program (collective bargaining agency or "union") but who do not report to and are not responsible to the officers of CNA; therefore be it

RESOLVED: That the Council of CSMS request its Committee on Allied Medical Services to study and report on the following:

(1) The relationships between various categories of nursing personnel; their respective status, designations and functions.

(2) The actual and potential effects of labor union-type activities by nurses on the care of patients and the discharge of professional responsibilities, the study to include, but not be limited to, consultation with the Connecticut Nurses' Association, the Connecticut League for Nursing, the Connecticut Society of Registered Nurses and the Connecticut Hospital Association.

(3) Other matters related to the foregoing.

Finally, it was VOTED to appoint Oliver J. Purnell, Rockville, to membership on the Committee on Allied Medical Services.

Request for Opinion re Organ Transplant Legislation

It was VOTED to refer to the Judicial Committee for study and report, a communication from Senator Jay W. Jackson, General Assembly, in which the Senator requested the Society's opinions on proposed legislation to amend the present statutes covering the donation of the body or parts thereof to include the legal questions raised by organ transplants (heart, kidney, etc.) from donors to recipients and a possible new definition of death. It is understood that the Judicial Committee may wish to consult with the Conference Committee with the State Bar Association in its study of these matters.

Progress Reports—Connecticut Regional Medical Program

(a) *Report of Ad Hoc Committee to Study CRMP "Revised Organizational and Operational Structure"*: After making several editorial changes in the text of the report, it was VOTED to accept the report as the Council's official position with respect to CRMP's new organizational and operating structure. Principally, in brief, the report calls for sixteen practicing physicians to represent organized medicine in Connecticut on the CRMP Advisory Board, eight designated by the Council and subject to recall and replacement and eight others designated by the component County Medical Associations on the basis of one per Association; further, that two members of the CRMP Executive Committee be practicing physicians designated by the Council. The eight physicians designated by the Council for service on the Advisory Board would be "chosen to represent various areas of special interest and practice, including general practice . . .". It was further VOTED to transmit this report to the Chairman of the CRMP Advisory Board with the request that the Board study the recommendations contained therein with a view toward incorporating same in the new organizational and operating structure of CRMP.

(b) *Report of CSMS Liaison Committee with CRMP*: The President, Norman H. Gardner, reported that, at the request of the Chairman of the CRMP Advisory Board, he had appointed a Liaison Committee with CRMP as follows: Norman H. Gardner, Chairman, Stevens J. Martin, Frank K. Abbot, Louis Rogol and Carl W. Johnson. The President reported further that the Liaison Committee had met with members of the CRMP Executive Committee on September 17, 1968, that discussion had been limited largely to the areas of CRMP "guiding philosophy and structure" and that arrangements were being made to review the differences of CSMS and CRMP on the program outlined in the Operating Grant Request at subsequent meetings. On behalf of Mr. Arthur Rogers, Chairman of the CRMP Advisory Board, he transmitted to the Council a request that the Society designate its presently authorized representatives (four members to the Advisory Board and one member to the Executive Committee) forthwith, in order that CSMS could have representation on the revised Advisory Board when the latter holds its first meeting within the next month.

Pursuant to acceptance of the Liaison Committee's report, the following actions were taken:

1. IT IS MOVED: That the Council of CSMS reaffirm support, in principle, of the concept of regional medical programs, and of those aspects of the Connecticut Regional Medical Program's Operating Grant Request of which it has already approved.

2. IT IS MOVED: That the Council of CSMS, in response to CRMP's stated urgency that the CRMP Advisory Board and Executive Committee be formed without delay and in order that the Society shall have immediate representation in the CRMP structure, designate four members of CSMS to serve as members of the CRMP Advisory Board and designate one of the four to serve on the CRMP Executive Committee; and it is further

MOVED: That the Council of CSMS inform the Chairman of the CRMP Advisory Board that such designations are made at this time solely for the reasons stipulated, and are not to be construed as acknowledgement that the Council is or will be satisfied with the limited representations of practicing physicians in the CRMP structure that is presently allowed.

3. IT IS MOVED: That the Council of CSMS, through its liaison committee with CRMP, offer to the CRMP Advisory Board an open-end, working committee of qualified CSMS members to assist in a detailed reorganization and re-planning of the CRMP Operating Grant Request, including deletion or replacement of those sections that demand it.

(c) *Reply to Communication from State Senator Shaffer*: Having received a letter from State Senator Gloria Shaffer expressing hope that the Society's differences with CRMP over the latter's Operating Grant Request would be resolved "speedily", and voicing her concern "with the need for comprehensive planning to insure the highest quality of medical care, the most efficient system of delivery, and the elimination of unnecessary costs . . .", it was VOTED to adopt the following motion:

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TROCINATE® 400 MG.
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Contraindications: Hypersensitivity to tetracycline.

Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.

Precautions: Nonsusceptible organisms may overgrow; treat superinfection appropriately. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Side Effects: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

Upon adverse reaction, stop medication and treat appropriately.

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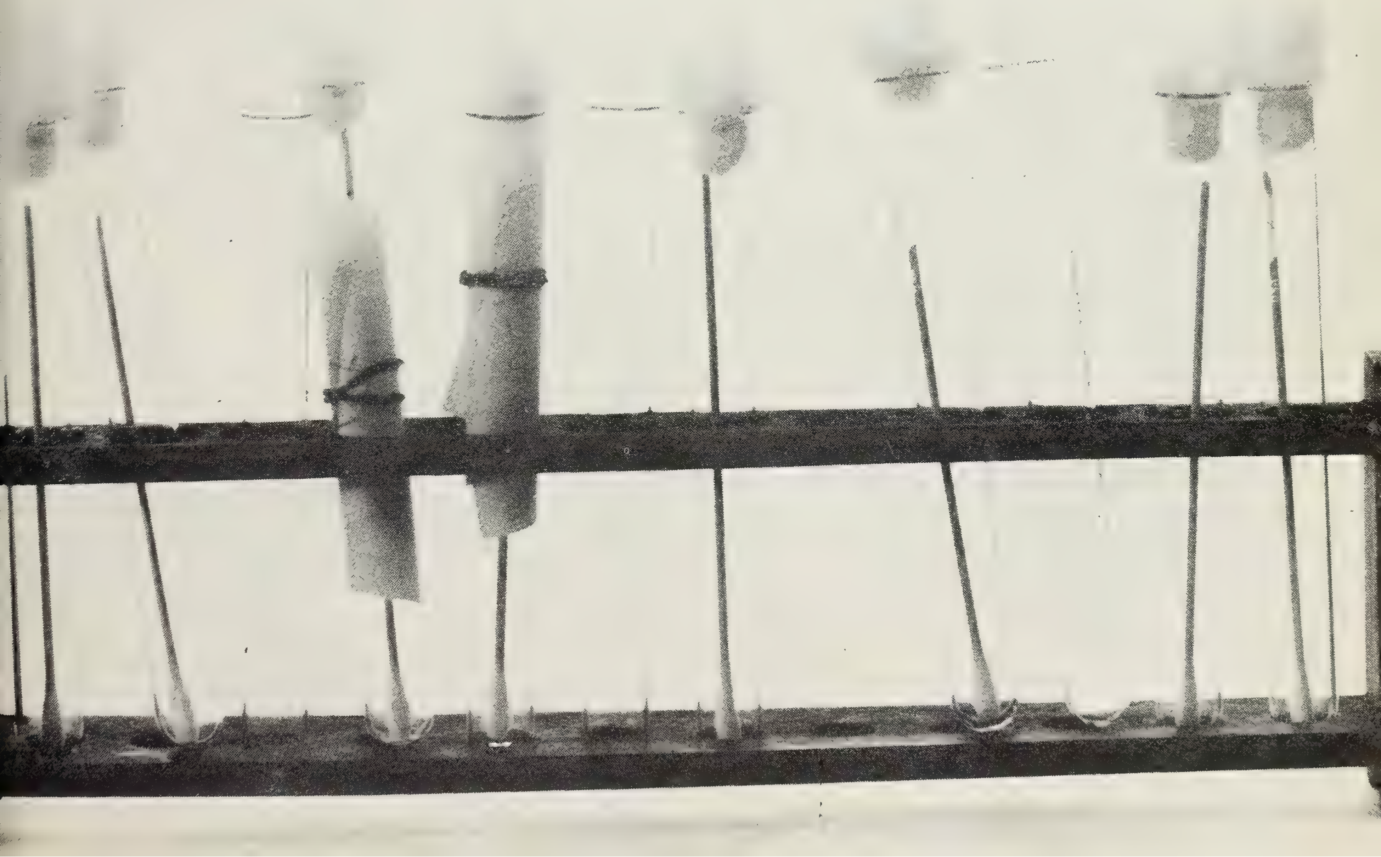

IT IS MOVED: That the Council of CSMS authorize the General Manager to send State Senator Gloria Shaffer, 14th District, copies of all evaluation materials of the CRMP Operating Grant Request transmitted by the Council to the National Institutes of Health on August 22, 1968, and to offer Senator Shaffer an opportunity to meet with CSMS representatives to discuss these materials if she so desires.

Meeting of October 10, 1968

The recessed meeting of September 25, 1968 was reconvened by the Chairman at 2:15 P.M.

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Caplan, Grendon, Weber, Jr., Abbot, Fabro, Bradley, Rogol, Cramer, Farrell, Petrie, Purnell, Shepard, J. Grant, Friedberg, McDonald, Pelz, Granoff, Wilson and Roch.

Also present were: Mrs. Lindquist, Dr. Hess, Dr. Patterson, Dr. Redlich, Mr. Villano and Dr. Richards.

Absent were: Drs. Brandon, Egan, Spitz, Nemoitin, Johnson, R. Grant and Palomba.

II. Routine Business

CSMS Dues Exemption

It was VOTED to exempt from payment of CSMS membership dues the following Active Member for the reason and period indicated:

Richard A. Smeraldi, Stamford (FCMA)—
Military Service—1968

Date of Next Meeting

The next meeting of the Council was scheduled for Wednesday, November 13, 1968.

III. Old, New and Special Business

Election of Student Members

It was VOTED to approve applications for Student Membership received from sixteen residents of Connecticut who are enrolled in medical schools in the United States. A list of those elected will be published in the Journal.

Request for Opinion—State Insurance Commissioner

In a letter dated September 5, 1968, Insurance Commissioner Cotter invited the Society to express "any comments or opinions it may have" on the proposed "Century Contract" of Connecticut Medical Service, Inc., which has been resubmitted by CMS for his approval. After reviewing the Council's earlier study of the proposed Contract (Feb.-Mar.), it was VOTED to send to the Commissioner as information a copy of an evaluation letter sent to the membership on February 29, 1968 and a copy of a commentary letter sent to the Commissioner on March 25, 1968. In brief, these documents pointed out that the proposed Contract did not embody the "usual, customary and reasonable charge" method of payment for physicians' services, and that the CSMS Relative Value Schedule had not been used in setting up the schedule of payments, both of which features are advocated by the Society. However, consistent with the earlier position taken, no recommendation concerning approval or disapproval of the proposed Contract was made to the Commissioner, to the membership, or to the public.

Letter of Recommendation re NHCMA Member

It was VOTED to receive as information, and with thanks, official notice that Luca E. H. Celentano, New Haven, has been commended by the State Commission for Higher Education for "the professional help which has been given (by Dr. Celentano) both to the Standing Committee on Accreditation of the Connecticut Council on Higher Education and to the Commission for Higher Education of the State of Connecticut". The letter describes Dr. Celentano's contributions as "thoughtful and extensive". It was further VOTED to make note of this commendation in these minutes and to publish same in the Journal.

Report—Liaison Committee with CG on Medicare B

Dr. Martin and Dr. Cramer gave brief verbal reports on some of the matters discussed with Connecticut General representatives at recent liaison meetings, including an account of an on-the-scene visit to CG's computer department at Bloomfield where Medicare B claims are analyzed to determine the prevailing levels of fees in the various "charge areas" throughout the state.

Progrm Offer—Health Insurance Council

It was VOTED to accept, with thanks, an offer of the Connecticut Health Insurance Council to arrange an educational program on health insurance policies (types, comprehensives, factors influencing design, price and sale, etc.) for a future Conference of County Medical Association Officers, and a corollary offer to underwrite the costs of a reception-dinner to follow the program. Because of previous commitments to subjects for such Conferences, it will be suggested that the Health Insurance Council plan to arrange this program for February, 1969.

Training Program for Surgical Technicians

It was VOTED to refer to the Committee on Allied Medical Services, for study and report, a proposal to set up an associate degree program for training surgical technicians, followed by certification and licensure, which was brought to the Council's attention by Dr. James H. Foster, Chairman of the Surgical Technology Committee, Hartford Hospital.

Council Directives on Legislative Questions

Acting on a series of Questions raised by the Committee on State Legislation and others, the Council VOTED as follows:

Therapeutic Abortion Statutes: To direct the Committee on State Legislation to draw up a bill for CSMS sponsorship at the 1969 General Assembly which would call for revision of the existing abortion statutes in accordance with the CSMS policy statement on same, be limited to same as to indication, and contain a reasonable residency requirement.

Gun Control Statute: To direct the Committee to voice the Society's opposition to any provision in any gun control bill that may come before the 1969 General Assembly which would require compulsory reporting by attending physicians and/or superintendents of mental institutions of any type of persons they believe "to be suffering from mental illness/mental retardation, alcoholism or drug dependence" to the State Police Commissioner.

Drug Control Statutes: To adopt a resolution introduced by the Committee on Mental Health as follows:

"RESOLVED: That the Council of CSMS sponsor pertinent legislation in the next session of the General Assembly to reduce the penalties for the possession and personal use of marihuana to the level consistent with the position taken by the AMA Council on Mental Health and its Committee on Alcoholism and Drug Dependency. The proposed legislation should contain amendments to Public Act 555 to change the penalty for possession and personal use of marihuana from that of a felony to that of a misdemeanor."

It was further VOTED that, pending receipt of legal interpretation of the existing statutes in this regard, implementation of the action proposed in the resolution be deferred.

Resolution—Principles re Delivery of Medical Services

A resolution titled: "Guiding Principles re Delivery of Medical Care Services", originally introduced at the meeting of August 29, 1968, was re-introduced in edited and rewritten form for Council consideration. After approving several amendments to one paragraph, it was VOTED to approve the statement of subject guiding principles and distribute same to a long list of individuals and agencies, both public and private, who have professed interest in the efficient delivery of high quality medical care to all persons living in the United States. For the membership of the Society, the statement will be published in an early issue of the Journal.

Proposed Amendments to the CSMS Bylaws

It was VOTED to approve, and to transmit to the next meeting of the House of Delegates for introduction and subsequent approval, proposed amendments to the Bylaws which would:

(1) Delete provision for a "Panel on Physician-Hospital Mediation", the duties of which have been assumed by the Judicial Committee.

(2) Rewrite several sections of Article X, having to do with Council-appointed Committees, subcommittees, representatives and advisors, so that the Council may appoint and dissolve such appointments, from time to time and on the basis of need, without the necessity of amending the Bylaws to do so.

(3) Make the "Committee on Disaster Medical Care" a Standing Committee of the House of Delegates and assign it to a Standing Divisional Board.

Connecticut Regional Medical Program

(a) Dr. Gardner and other members of the Liaison Committee with CRMP reported on the deliberations of several joint meetings held with CRMP representatives. In brief, it was reported that joint review of a number of sections of the Operating Grant Request had been accomplished, in particular those to which the Council had given approval or voiced any minor objection. Another meeting has been scheduled at which this review will be continued, moving on to those sections on which the Council had voiced major objection or had disapproved in their entirety. While some degree of "meeting of the minds" has appeared to result from the discussions to date, the Council was advised to await receipt of printed material from CRMP confirming that accommodations to the Council's positions had been made before giving approval to any of them. In this regard, it was further VOTED to request CRMP to furnish the Council with copies of any supplementary material (to the original Operating Grant Request)

Knee-deep

TA-6008

in osteoarthritic pain

If aspirin doesn't help, move in vith Tandearil.

The trial period is brief: 1 week. Try one tablet q.i.d. at first. Tandearil usually starts working within 3 to 4 days. Vhen response occurs, as little as 1 or 2 tablets daily may hold back pain and stiffness, and increase joint motion.

On the next page is a summary of adverse reactions, contraindications, varning and precautions.

Tandearil.
It can help get his mind off his knee.

Please review full Prescribing Information carefully before prescribing.

For osteoarthritic knees, spines, shoulders, hips, etc.:

Tandearil®
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Tandearil, oxyphenbutazone:
For brief summary see next page.

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Tandearil®
oxyphenbutazone

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.

Warning: This drug is an analog of phenylbutazone; sensitive patients may be cross-reactive. If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Persistent or severe dyspepsia may indicate peptic ulcer; perform upper gastrointestinal x-ray diagnostic tests if drug is continued. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with caution in the first trimester of pregnancy, and in patients with thyroid disease.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patients should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia), sudden weight gain (water retention), skin reactions, black or tarry stools or other evidence of intestinal hemorrhage occur. Make complete blood counts at weekly intervals during early therapy and at 2-week intervals thereafter. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The more common are nausea and edema. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension, the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately after meals or with milk to minimize gastric upset. Drug rash occasionally occurs. If it does, promptly discontinue the drug. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), or a generalized allergic reaction similar to a serum sickness syndrome may occur and require permanent withdrawal of medication. Agranulocytosis can occur suddenly in spite of regular, repeated normal white counts. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, hypersensitivity angiitis, pericarditis and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur

Dosage in Osteoarthritis: Initial: 3 to 6 tablets daily in divided doses. Usually unnecessary to exceed 4 tablets daily. A trial period of one week is considered adequate to determine the therapeutic effect of the drug. Maintenance: Effective level often achieved with 1 or 2 tablets daily, should not exceed 4 tablets daily.

In selecting appropriate dosage in any specific case, consideration should be given to the patient's weight, general health, age and any other factors influencing drug response.

Availability: Tan, round, sugar-coated tablets of 100 mg. in bottles of 100 and 1000.
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that CRMP plans to submit to the National RMP Advisory Council *before* the holding of the site inspection or *before* it is sent to the National Institute of Health, whichever of these actions to submit supplementary material on the Grant Request is scheduled to be carried out first.

(b) Since there appears to be some confusion about the activities of the CRMP Task Forces, past and present, it was VOTED to request CRMP to furnish the Council with up-to-date information as to the composition and activities of all Task Forces at the present time, especially as to the representation of practicing physicians on each of same. It was further VOTED to request the Chairman of the CRMP Advisory Board to furnish the Council with copies of all Task Force reports and recommendations that are said to be reflected in the text of the Operating Grant Request.

(c) After extended discussion, it was VOTED to designate members of the Society to serve on the CRMP Advisory Board and Executive Committee as follows:

Advisory Board

Norman H. Gardner, East Hampton, President
Stevens J. Martin, Hartford, President-Elect
Max Caplan, Meriden
Carl W. Johnson, Thompsonville

Executive Committee

Norman H. Gardner, East Hampton, President

It was further VOTED that, in the letter notifying CRMP of these designations, there be a restatement of the Council's previously adopted position; i.e., that the making of the designations at this time is "not to be construed as acknowledgment that the Council is, or will be satisfied with the limited representation of practicing physicians in the CRMP structure that is presently allowed".

(d) It was VOTED to receive as information notice that Senator Gloria Shaffer and her Hospital Study Committee (of the General Assembly) will meet on October 29, 1968 with the members of the CSMS Liaison Committee with CRMP to discuss the Society's position on the CRMP Operating Grant Request and related matters.

Resolution—LCMA

It was voted to adopt a resolution, introduced by the Executive Committee of the Litchfield County Medical Association, which reads as follows:

"RESOLVED: That the Council of CSMS (arrange to) publish a monthly newsletter, with copies to be mailed to all members of the Society."

Since neither the resolution nor its letter of transmittal to the Council offered any information as to what type of newsletter was intended thereby, appropriate inquiry regarding same will be made of the LCMA Executive Committee.

Appointment to State Advisory Committee on Hospital Licensing

It was VOTED to appoint Christie E. McLeod, Middletown, to succeed herself as a member of the Advisory Committee on Hospital Licensing for a five-year term, October 1, 1968-September 30, 1973. In accordance with Section 19-31 of the General Statutes, the Society is privileged to nominate one member of this State Advisory Committee.

Support of Resolution—AMA House of Delegates

Having been informed that the North Carolina Delegation (and perhaps others) will introduce a resolution at the forthcoming Interim Meeting of the AMA House of Delegates that will urge the AMA to take appropriate action to authorize the formation of an American Board of Family Practice, the Council VOTED to instruct the CSMS AMA Delegates and Alternate Delegates to support such resolution(s) in principle.

Request for Sponsorship—Educational Program on Marijuana

It was VOTED to give Society sponsorship to this Educational Program (November 16, 1968) which is being arranged by the State Drug Advisory Council and is being co-sponsored by the American Chemical Society, the Connecticut District Branch of the American Psychiatric Association, and St. Joseph's College, West Hartford. No financial support of the Program was requested.

Memorializing Stamp for William Beaumont, M.D.

It was VOTED to cooperate with the State Medical Societies of Michigan, Wisconsin, Vermont and Missouri in seeking to obtain from the five respective state legislatures memorializing resolutions which call for the Postmaster General to issue a special stamp in 1972 honoring William Beaumont, M.D., on the sesquicentennial of his "great discovery" in gastric physiology (1822) while serving as Post Surgeon at the fort on Mackinac Island, Michigan. Dr. Beaumont was born in Lebanon, Connecticut in 1785. To this end, it was further VOTED to direct the Committee on State Legislation to have drafted and sponsor the introduction of an approprite memoralizing resolution at the 1969 General Assembly. Frederick C. Weber, Jr., CSMS Secretary, volunteered to arrange for members of the General Assembly (House and Senate) to introduce jointly such a resolution on behalf of the Society.

Proposed Congressional Cutback in Medicaid Funds

Having been apprised that a bill amending Title XIX to reduce the Federal share of Medicaid costs in Connecticut from 50% to 25% and place stringent limits on Medicaid eligibility is now in the House-Senate Joint Conference Committee, the Council VOTED to urge (by letter) the two Senators and six Representatives from Connecticut to vote against such amendments in order that the financial status of Medical Assistance in this state will not be jeopardized and/or the Medicaid Program made totally inadequate.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on September 25 and October 10, 1968. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

DIABETES WEEK IN CONNECTICUT

Dr. Philip Bondy, C.N.H. Long Professor and Chairman, Department of Internal Medicine, Yale University School of Medicine, will inaugurate Diabetes Week in Connecticut which will be observed nationally November 17-23.

Dr. Bondy will address a joint meeting of the Connecticut Diabetes Association and the New Haven Medical Association Wednesday evening November 20 at 8:15 p.m. in the auditorium of the New Haven Medical Association, 364 Whitney Avenue, New Haven, Connecticut. His topic will be "Therapeutic Lessons from Long Lived Diabetics".

The Connecticut State Medical Society offers placement assistance through the Physician Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

Welcome, New Members

Hartford County Medical Association

James R. Abel, M.D., 300 Kensington Avenue, New Britain, Conn. 06050.

Peter R. Amato, M.D., 21 Woodland Street, Hartford, Conn. 06105.

Peter E. Barwick, M.D., Avon Professional Center, Avon, Conn. 06001.

Robert H. Berland, M.D., 60 Gillett Street, Hartford, Conn.

Stanley H. Bernstein, M.D., Mount Sinai Hospital, Hartford, Conn. 06112.

John P. Callan, M.D., 801 Farmington Avenue, West Hartford, Conn. 06119.

Richard M. Dauphinais, M.D., St. Francis Hospital, Hartford, Conn. 06105.

Leonard A. DeFusco, M.D., 60 Gillett Street, Hartford, Conn. 06105.

John B. Franklin, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Edward J. Fredericks, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Albert L. Geetter, M.D., 21 Woodland Street, Hartford, Conn. 06105.

Kenneth M. Godlash, M.D., 711 Cottage Grove Road, Bloomfield, Conn. 06002.

Thaddeus J. Gutkowski, M.D., 350 Farmington Avenue, Hartford, Conn. 06105.

Carl F. Hinz, Jr., M.D., Univ. Conn. Sch. of Medicine, Hartford, Conn. 06105.

Jules S. Hollander, M.D., 5 North Main Street, Thompsonville, Conn. 06082.

Alan F. Krupp, M.D., 15 West Middle Turnpike, Manchester, Conn. 06040.

William B. Lehmann, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Irwin H. Lepow, M.D., Univ. Conn. Health Center, Hartford, Conn. 06105.

Martha L. Lepow, M.D., Univ. Conn. McCook Hospital, Hartford, Conn. 06112.

Philip H. McClure, M.D., 300 Main Street, Bristol, Conn. 06010.

Guy Owens, M.D., McCook Hospital, Hartford, Conn. 06112.

David M. Satlof, M.D., 50 Gillett Street, Hartford, Conn. 06105.

Ralph C. Secor, M.D., 140 Garden Street, Hartford, Conn. 06105.

Stephen H. Sherman, M.D., 2 Holcomb Street, Hartford, Conn. 06112.

William P. Slover, Jr., M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Betty J. Hannon, M.D., 89 North Street, Bristol, Conn. 06010.

Frederick W. Sunderman, Jr., M.D., McCook Hospital, Hartford, Conn. 06112.

Robert C. Thomas, M.D., McCook Hospital, Hartford, Conn. 06112.

Placement Opportunities

SENIOR PHYSICIAN—Openings for Senior Staff physician — $16,370-$19,970. Many liberal fringe benefits. Live-in at minimal cost. Write Veterans Home and Hospital, Rocky Hill, Connecticut or call 529-3571, Ext. 395.

HOUSE PHYSICIAN — FULL TIME — to cover Emergency Room and house calls. Night coverage, five nights a week, 6 P.M. to 7 A.M. Must have Connecticut license. $20,000 a year with apartment; good fringe benefits. Minimum contract one year. Write P.O. Box 3494, Bridgeport, Connecticut 06604.

CONNECTICU T —PSYCHIATRIST, CHIEF OF PROFESSIONAL SERVICES needed for a community-oriented mental hospital; will develop, direct and coordinate all clinical services in 1600-bed geographically decentralized hospital; review and modify operating criteria for standards of service; coordinate clinical treatment, training and research activities, OPD, day-care, in-patient consultation and emergency services included; opportunity for association with Wesleyan and Yale Universities and UConn. Starting salary commensurate with training and experience; liberal fringe benefits. All particulars should be sent in first letter to M. K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

ANESTHESIOLOGIST—to associate with another anesthesiologist at the World War II Veterans' Memorial Hospital, Meriden, Connecticut. For further information, contact Marvin Albert, M.D., World War II Veterans' Memorial Hospital, Paddock Avenue, Meriden, Connecticut 06450 or telephone 237-5531.

G.P.—Terminating large general practice of 30 years on October 1, 1968, to assume Emergency Room duties at the New Britain General Hospital. Interested in finding physician to take over practice. Contact immediately: Roger T. Scully, M.D., 55 West Main Street, New Britain, Connecticut 06051. Telephone (203) 223-0251.

PEDIATRICIAN for a rapidly growing community in Western Connecticut. Present pediatrician wants to concentrate solely on subspecialty. Arrangements on solo, salary or associate basis.

EMPLOYEES' PHYSICIAN — physician for employees' clinic, whose duties would consist of pre-employment and annual physical examinations, daily sick call, and occasionally immunizations, hours from 8:00 a.m. to 5:00 p.m. with an hour for lunch, Monday through Friday. Four weeks' vacation after one year and excellent fringe benefits. Salary of $20,000 per annum.

PEDIATRICIAN—Three member partnership on Obstetrics and Gynecology is looking for a pediatrician for the Enfield, Connecticut area which serves a population of 60,000. An office immediately available in a new air-conditioned Medical Building.

Placement Wanted

INTERNIST—Board eligible with cardiology subspecialty; 14 years private practice in Connecticut, also administrative and teaching experience. Will consider group, hospital or industrial position, clinical or administrative.

INTERNIST — 41 year old internist-cardiologist seeks association with group, industry or institution. Has specialty training, also, in chest diseases and dermatology. Connecticut license.

INTERNIST—Board certified with subspecialty of hematology, wishes to practice in a hospital, in laboratory work and patient care. Would like at least part or full-time hospital practice. Has National Boards and is available in October 1968.

ANATOMIC PATHOLOGIST — Board eligible with Connecticut license. Would like to practice with an associate. Available immediately, 32 years of age.

PATHOLOGIST—34 years of age, Board certified, has applied for Connecticut license. Would like to practice in a hospital or in private practice. Available as of November 1, 1968.

INTERNIST—Subspecialty in Infectious Diseases, recently completed residency, desires association of Group Practice.

NEUROLOGIST & PSYCHIATRIST—Board certified in both specialties, desires association with individual or group in Eastern Connecticut.

OBS-GYN—Board eligible, military obligations completed, wishes associate practice starting July, 1969. 30 years of age, married and has National Boards.

G.P.—Physician, age 30, military obligation completed, desires general practice or Emergency Room slot in Connecticut. Available immediately. Has Connecticut license and National Boards.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

COUNCIL ADOPTS STATEMENT ON DELIVERY OF MEDICAL CARE SERVICES

On October 10, 1968, the Council voted to adopt a resolution submitted by the Committee on National Legislation which embodies a series of "guiding principles" that have been established by the Society's House of Delegates over the past decade. Reprints of the resolution will be funished to a substantial number of individuals and agencies that profess interest in the efficient delivery of high quality medical care to all Americans. The text of the resolution is published below for the information of the membership.

RESOLUTION

SUBJECT: GUIDING PRINCIPLES RE DELIVERY OF MEDICAL CARE SERVICES

WHEREAS: The number of parties, public and private, which profess interest in the efficient delivery of high quality medical care to all persons living in the United States is increasing year by year; and

WHEREAS: It is recognized that each of these interested parties must actively seek and maintain close communication and consultation with the others if the common goal is to be pursued cooperatively and for the benefit of all people; and

WHEREAS: The practicing Doctor of Medicine, duly licensed, is the prime deliver of patient care in the United States today and, hence, is intensely interested in all proposals that may be advanced as possible methods of improving the American health care system, whether such proposals are initiated by his own professional organizations or by other interested parties; and

WHEREAS: Independent or unilateral actions proposed or implemented in this field by legislators, so-called "consumer" groups and/or health planning agencies that do not take into full account the opinions and professional expertise in patient care of practicing physicians are prone to be theoretical in concept and not in keeping with time-tested medical principles which have received wide public acceptance; and

WHEREAS: The Connecticut State Medical Society is the representative professional organization of more than 3800 licensed Connecticut physicians, approximately 80% of whom are engaged in the private practice of medicine; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society reaffirm certain basic principles regarding the delivery of high quality medical care, established by the Society's House of Delegates over the past decade, as follows:

(1) That communication and consultation with the Society be readily available at all times to all responsible parties having an interest in matters relating to the delivery of medical care services and to the public health.

(2) That medical care of uniformly high quality be available to all persons living in the United States, without exception.

(3) That the maintenance of high quality in medical care is of paramount importance, and that all other considerations are secondary to this goal.

(4) That it is the responsibility of each practicing physician to help limit the total cost of health care by rendering and prescribing only those medical goods and services which are necessary to optimum care of his patients.

(5) That the practicing Doctor of Medicine, duly licensed, is the prime deliverer of patient care to the people of the United States and has, with his colleagues, the responsibility of assuring that such care is of high quality.

(6) That each practitioner, as an individual, is directly accountable for his professional acts and deportment to his patients, to his medical peers and to authorized licensing agencies, and that the public interest is well protected by such accountability; further, that lay (non-physician) control of, or interference with, professionally approved medical care policies and ethical practices is contrary to the public interest and should be prohibited by law at all levels of government.

(7) That whether medical services are provided by physicians engaged in solo, partnership or group practice, and irrespective of what method for financing such services obtains, the patient must have freedom to choose his attending physician from among all those qualified and available in and to his community area of residence; the physician, except for emergency situations, must have freedom to accept or not to accept a patient into his professional care; and the patient's attending physician, with the patient's consent, must have freedom to select consultants among all those qualified and available in and to his community area of practice. Assignment by any third party of patient to physician or physician to patient, made without freedom of choice, is in violation of this principle and cannot be approved.

(8) That units of organized medicine preferably at the county medical association level, shall have in being appropriately constituted committees which are readily available to all responsible sources to receive, review and render peer judgments on all questions having to do with medical ethics, the professional acts and fees of physician members, and the proper utilization of medical and related services rendered and/or prescribed by member physicians in the treatment of their patients.

(9) That, if self-employed in a solo, partnership or group practice setting, the physician is entitled to receive from his patient, or on behalf of his patient from a third party, payment of his self-determined, usual (full) fees for services properly rendered, provided that such usual fees are reasonable in that they fall within the levels of charges obtaining in his community area of practice among a substantial majority of physicians of equivalent qualifications for equivalent services rendered. Corollary to this principle is the guarantee of organized medicine (in Connecticut, the State Medical Society) that if a physician's fee is questioned by the patient or by any other party legitimately concerned with the rendering of the service to the patient, such question shall be received and processed by the county medical association, as outlined in preceding paragraph (8), and that the judgment of the association shall be binding upon the member.

Doctor's Office

A. Reid Allison, M.D., announces the opening of an office for the practice of internal medicine at 45 South Main Street, West Hartford.

Charles E. Morhardt, M. D., announces the opening of an office for the practice of general surgery at 45 South Main Street, West Hartford.

Beverly Pass, M.D., announces her association with that of her husband, John M. Pierce, M.D. for the practice of pediatrics in the Winsted Memorial Hospital Medical Building, 71 Spencer Street, Winsted.

David P. Tyrrell, M. D., announces the opening of an office for the practice of pediatrics at 85 Jefferson Street, Hartford.

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Special Article

Endocrine Effects of Psychotropic Drugs: VI. Male Sexual Function

Richard I. Shader, M.D., and Alberto DiMascio, Ph.D.

The interest of clinicians in the effects of psychotropic drugs on male sexual functions has resulted largely from a concern for non-endocrine drug effects. Impotence, decreased libido, and ejaculation disorders have been reported. Singh[1] in 1961, commented on the failure of ejaculation in males taking thioridazine while erection and orgasm were unaltered. This pattern was identical to the effects produced by dibenzyline which Green and Berman[2] had reported in *Connecticut Medicine* in 1954. Shader[3] suggested that this ejaculation disorder is the result of central sympathetic (hypothalamic) depression and peripheral alpha adrenergic blockade. Similar ejaculation problems have been reported for chlorprothixene[4] and pargyline[5].

Shader and Grinspoon[6] observed true oligospermia in a small number of male chronic schizophrenic patients and questioned whether these findings were related to previous phenothiazine or reserpine ingestion. Their report includes a review of the literature on animal studies using phenothiazine derivatives. These animal studies, conducted in a variety of non-primates and primates, suggest that the phenothiazines and reserpine inhibit or suppress hypothalamic and pituitary function which results in increased prolactin production and/or decreases in the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH), or interstitial cell stimulating hormone (ICSH). Many changes in animals have been reported following phenothiazine administration ranging from no effect or a reduction in the percentage of motile sperm to regressive and atrophic changes in the testes such as degeneration of the seminiferous tubules and impaired spermatogenesis.

Shader, Taymor, and Grinspoon[7] studying ten male chronic schizophrenic patients, five on placebo and five on thioridazine, found no significant drug effect on urinary follicle stimulating hormone levels. However, significant differences were found between those subjects who had shown early or preadolescent symptomatology, and those whose symptoms began in late adolescence. These groups correspond roughly to "process" and "reactive" clinical history categorizations. Those patients who had had an early onset of symptoms had absent to low FSH levels, while those with onsets in late adolescence had FSH values within the normal range. Similarly, among those patients who showed, at the time of study, more schizophrenic disorganization—regardless of the thioridazine or placebo distinction—there were lower FSH levels. This latter finding is consistent with the work of Suwa, *et al*[8] which we noted in an earlier paper in this journal[9]. In a longitudinal study Shader, Taymor and Grinspoon[10] followed the thioridazine patients mentioned above and found no significant differences among the on-drug, off-drug, and return to drug levels of FSH and total gonadotropins.

Rasmussen and Johnsen[11] found that long-term administration of chlorprothixene in daily doses of more than 100 mg to three male schizophrenic patients caused a fall in urinary gonadotropin excretion. Two additional patients with reduced or absent pituitary function secondary to operations for craniopharyngiomas showed increased urinary gonadotropins following chlorprothixene, chlorpromazine, haloperidol, or meprobamate. These increases appeared on the second through sixth days of drug administration and were transient in character. Imipramine and amitryptiline did not produce such increases.

Blair, Simpson, and Kline[12] found that the monoamine oxidase inhibitor, phenelzine, pro-

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DR. RICHARD I. SHADER, Assistant Professor of Psychiatry, Harvard Medical School; Lecturer in Social Relations, Harvard University; Senior Research Psychiatrist and Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, Boston, Mass.

ALBERTO DIMASCIO, PH.D., Research Associate in Psychiatry, Harvard Medical School; and Co-Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, Boston, Mass.

duced increased spermatogenesis in the depressed males. Simpson, Blair and Cranswick[13] studying the butryophenone derivative, WY-3457, found polyspermia in seven of nine cases, and necrospermia in three of these same patients. Five of the remaining six patients had low sperm motility. All of the patients with abnormalities in spermatogenesis showed improved spermatogenesis once the drug was discontinued. In a subsequent study Simpson, *et al*[14] found that trimiprimine produced an ejaculation disorder, and that in a few patients the ejaculates contained no sperm or low volume and counts.

Very few longitudinal investigations of the effects of psychotropic drugs on gonadotropin excretion and sperm production have been carried out. From the limited data reviewed here, it is not possible to draw conclusions. Further investigation is essential. It seems reasonable to urge caution in the use of large doses of psychotropic drugs in preadolescent males, since these drugs could potentially alter or modify the sequence and balance of endocrine mechanisms essential to normal puberty.

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The superior man blames himself,
The inferior man blames others.

None so old than he who hopes for a year of life.

An old man is a bed full of bones.

Save something for the man that rides the white horse—old age.

Use legs and have legs.

Young men think old men fools, and old men know young men to be so.

The glory of young men is their strength, and the beauty of old men is the hoary head.

Bible (*Proverbs* 20:29)

COUNCIL STATEMENT ON CRMP OPERATING GRANT REQUEST

The following "Summary Statement" of the Council on the Operating Grant Request of the Connecticut Regional Medical Program was sent in late August to the National Advisory Council, Division of Regional Medical Programs, National Institutes of Health, along with copies of the report of its Ad Hoc Committee on CRMP Operating Grant Request and other supporting materials. The National Advisory Council has "deferred action" on the 5-year, $24 million Grant Request until November, at which time it hopes to receive assurance that "cooperative arrangements" between all concerned Connecticut health agencies have been worked out.

SUMMARY STATEMENT OF THE COUNCIL OF THE CONNECTICUT STATE MEDICAL SOCIETY SUBJECT: CRMP OPERATIONAL GRANT REQUEST

Since 1966, the Connecticut State Medical Society has endorsed wholeheartedly the stated objective of P.L. 89-239 which is, in brief, to seek to improve patient care in the fields of heart disease, cancer, stroke and related diseases through the medium of grant-supported regional programs of education, training, research and demonstration. In addition, the Society has advocated strongly that this worthy objective be met, as the Congress clearly intended (Section 900 (c) of P.L. 89-239), "without interfering with the patterns, or methods of financing, of patient care or professional practice, or with the administration of hospitals, and in cooperation with practicing physicians, medical center officials, hospital administrators, and representatives from appropriate voluntary health agencies".

The Connecticut State Medical Society serves as a voluntary, non-profit, representative organization for some 3800 Connecticut physicians who are engaged in all types of health and health-oriented activities. More than 80% of the members are engaged in the private practice of medicine, either as individuals or in physician-managed associations. It is estimated that approximately 90% of Connecticut residents receive their personal health services in a private practice setting, whether in the doctor's office, in the home or in a hospital-type facility.

Hence, it is understandable that the Society has a special concern that the Connecticut Regional Medical Program be planned, developed and implemented "in cooperation with practicing physicians", and that the Program be directed intelligently toward improving patient care at the local level without interfering with existing patterns of professional practice or existing relationships between private practitioners and their patients.

To this end, the Society has recommended strongly that, through practicing physician representatives, it be given a "partnership" status in the program which is commensurate with the size of the private practice segment of its membership and the recognized importance of the private practitioner as the prime deliver of medical care in the Connecticut region.

On May 1, 1968, the House of Delegates of the Connecticut State Medical Society directed its Council (Executive Committee) "to seek from the Connecticut Regional Medical Program a review and reevaluation of the latter's structure and goals", and, soon thereafter, the Council appointed an Ad Hoc Committee to Study CRMP Operational Grant Request of March 1, 1968, and arranged for conferences with representative members of the CRMP Advisory Board, including the Deans of the Yale University and University of Connecticut Medical Schools. Subsequent to the consummation of this study and these conferences, on August 21, 1968, the Council adopted unanimously the report of its Ad Hoc Committee.

Based on the conclusions and the recommendations which appear in the report adopted, the Council has reached the following general conclusion as to the structure, development, guilding philosophy and goals of CRMP as of August 21, 1968:

CONCLUSIONS

(1) The Council concludes that, almost from the outset, major segments of CRMP's "planning design" have been developed to the point of proposed implementation on an elaborate scale without adequate study having been made of the multitude of excellent health care resources already available in Connecticut or adequate assessment having been made of unmet health care needs that may exist at

the community or "grass roots" level throughout the state. In particular, the Council is of the opinion that too much of the planning has been done by persons who, although acknowledged to have expertise in their own limited special fields, are not directly concerned with the provision of health services to patients and whose over-all orientation is such as to favor a system of centralized, academic and theoretical management of medical affairs; and, further, who evidently contemplate using non-voluntary "leverage" to impose that system on the Connecticut professions and public from above downward.

(2) In general, the Council finds that the proposed CRMP programs of which it approves (in principle, in part or in whole) are those which have been developed in reasonably close cooperation with representatives of private medical practice and associated health disciplines who have firsthand knowledge of the day-to-day problems encountered in delivering health care to thousands upon thousands of patients with differing individual needs, personalities, intellects and responses.

(3) In general, also, the Council finds that the proposed CRMP programs of which it most strongly disapproves are those which appear to have been developed more or less independently by "planning experts" associated with the Program in executive or consultant capacities. In the Ad Hoc Committee's report, several such programs are categorized as reflecting pre-conceived "foreign", "alien" or "imported" concepts, meaning that they have been described at length in the earlier writings of CRMP staff members, consultants and similar "experts" and have not necessarily been evolved to accommodate to needs established by adequate study of the Connecticut health care scene. In this regard, the Council cannot agree with CRMP's sweeping statement that "there exists a climate of dissatisfaction in Connecticut with many aspects of the medical care system as it currently functions . . ." and has failed to obtain any satisfactory documentation of that statement from members of the Program's Advisory Board. The Council makes no claim that the existing system is without fault, but considers that these types of "shot-gun" programs would be more suitable for implementation in an underdeveloped nation abroad or a medically deprived area of this country, and, hence, should be delayed for implementation in Connecticut until much more is known about their suitability to this region.

(4) Concerning the proposed expansion of CRMP's "core staff", especially in the light of the foregoing, the Council is deeply disturbed by the possibility that such a staff, with millions of tax dollars at its disposal, might become a centralized bureaucracy with the statutory authority to mold, direct and control the patterns of health care for the entire state. While the intent to bring such a situation about will undoubtedly be denied by those directing the Program up to now, and may not exist at all, the Council is not reassured by reading in the Grant Request that, if all goes as planned, the voluntary agencies may be challenged ultimately by CRMP to make a decision to pursue their own "self-interests" independently or join with the Program to participate "as part of a larger common effort with a broad objective of public service (as determined by CRMP) . . .". Neither is it reassuring to read that "if the core staff is able to articulate convincingly the interests of the public as a whole, it will be able to maintain a stance which will be recognized as transcending individual interests." The Council is convinced that such authority is contrary to the intent of the Congress, and that it could not be exercised by the core staff without "interfering with the patterns, or methods of financing, of patient care or professional practice . . ." in Connecticut on an ever-increasing scale.

(5) As a corollary to (4) preceding, the Council believes strongly that the directions which CRMP will take in the future should be determined primarily by the Advisory Board, *not* the core staff, and that there should be substantial representation of private medical practice on the Advisory Board, amounting to at least one-third of the Board's membership, in order that the responsible coordinator of all medical care — the patient's attending physician — shall have an adequate voice in what is planned by CRMP and what programs are put into operation. In the Council's judgment, for CRMP to place continued major emphasis on the "above-downward" approach to advancing professional education and improving patient care in Connecticut would be most unwise and would almost guarantee widespread non-acceptance in many parts of the state.

(6) Finally, the Council wishes to make it clear that its evaluation of CRMP's proposed operational projects is intended to be constructive, not destructive. The Connecticut State Medical Society is on record as supporting the objectives of P.L. 89-239, and as pledging its full support, past, present and future, to all workable programs which will enable medical practitioners to deliver the highest quality of medical care to their patients.

OBITUARY

Philip M. Cornwell, M.D.
1909-1968

Dr. Philip Morba Cornwell died on August 23, 1968 in the Hartford Hospital as the result of overwhelming malignant disease that had become manifest less than three months previously. His friends, patients and colleagues are grateful that Phil was spared the torments of a long and excruciating struggle for survival.

Phil Cornwell was born in Hartford and received his preliminary education in the Hartford Public Schools. He was a graduate of Trinity College, Class of 1930, and Yale Medical School 1934. He received his internship training at Hartford Hospital from 1934-1936. After four years of general practice he entered the field of urology, serving as resident in that specialty at the Wisconsin General Hospital. He was instructor and professor of urology from 1943-1946 at the University of Wisconsin School of Medicine. Since his return to Hartford in 1946 until his death, he was a member of the Attending Staff of the Hartford Hospital in urology, and at the time of his death he was president of the Medical Staff to which position he had been elected for three consecutive years. Dr. Cornwell was a member of the Board of Directors of the Hartford County Medical Association for twelve years and was president of that organization in 1958 and 1959. In these positions of leadership his sincerity and steadfastness were a bulwark for those with whom he worked.

He was a very able and highly respected physician serving as consultant in his chosen field to a number of Connecticut hospitals.

Phil had many attributes, but above all he was a sensitive human being which, combined with a social disposition, won for him a host of grateful patients and a multitude of friends.

A fitting memorial to Philip M. Cornwell, my good friend and colleague, is the certain knowledge that he will continue to live in the minds and hearts of his contemporaries.

Edward H. Truex, M.D.

In Memoriam

Bucciarelli, John A.—Norwalk, Temple University School of Medicine, 1931. Dr. Bucciarelli was a practicing eye, ear, nose and throat specialist in New Canaan for 40 years. He was a New Canaan police surgeon, the town's health officer, and a member of the Board of Finance. He was a member of the New Canaan Physicians Association, the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the Connecticut Opthalmological Society. Dr. Bucciarelli died September 18, at the age of 63.

Frothingham, John G.—New Canaan, Harvard School, 1935. Dr. Frothingham was a pediatrician in the New Canaan area for over 25 years. He was a member of the New Canaan Physicians Society, the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, the New England Pediatric Society, and the Hezekiah Beardsley Pediatric Society. Dr. Frothingham died September 14, at the age of 60.

Locke, Harry L. F.—West Hartford, Tufts University School of Medicine, 1912. Dr. Locke was a pediatrician in the Hartford area for over 50 years. He was on the consultant staff at St. Francis Hospital. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Pediatric Academy. Dr. Locke died August 5, at the age of 81.

McGrath, John F.—West Hartford, McGill University Medical School, 1923. Dr. McGrath had practiced in the Hartford area for many years. He was a member of the surgical staff of St. Francis Hospital and McCook Memorial Hospital where he was president of the staff for several years. He was a member of the Hartford Medical Society, the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. McGrath died September 25, at the age of 71.

Stretch, James E.—Simsbury, George Washington Medical School, 1928. Dr. Stretch was a general practitioner in Simsbury for over 20 years. He was a Diplomate of the National Board of Medical Examiners. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Academy of General Practice. Dr. Stretch died June 9, at the age of 68.

NEWS BRIEFS

1. **FETAL EKG.** The world's first fetal intensive care unit featuring a unique electronic system for protecting unborn babies during the critical hours just before and after delivery has been opened at Yale-New Haven Hospital. The equipment is designed to detect fetal distress by electronically monitoring patterns of fetal heart rate in relations to uterine contraction during labor. Monitoring devices in the labor rooms provide a fetal electrocardiogram on a scope, an instantaneous fetal heart rate meter reading, and a continuous paper record of the heart rate and the uterine contractions.

2. **MEDICAL CARE EXPENDITURES.** The Tax Foundation reports that public spending for medical care has nearly doubled since the passage of Medicare and Medicaid in 1965. Federal and local governments spent $12.6 billion last year, compared with $6.7 billion in 1964. Private spending for medical care in the same period increased from $24.2 billion to $28.8 billion, as more of the burden was taken up by the public sector. To date, the Foundation points out, the major demonstrable effect of the legislation creating Medicare and Medicaid has been a shift in financing medical care from the private to the public sector.

3. **ER SERVICE.** Meriden Hospital has employed four physicians to staff its new Accident and Emergency Department on a 24-hour year-round basis. According to an announcement from the hospital, "these doctors have given up private practices to accept careers with the new concept of emergency specialization. They subscribe to the opinion in medical circles that full-time emergency and accident room coverage is not only desirable, it is a necessity."

4. **REGIONAL MEDICAL PROGRAM.** The following editorial appeared in the October 7 edition of the New Haven Journal-Courier: "A MEDICAL CONFLICT TO SETTLE. The Citizens of Connecticut have much to gain by swift settlement of the argument between the Connecticut Regional Medical Program and the Connecticut State Medical Society.

   "The conflict results from understandable and traditional distrust of bureaucracy by members of the Medical Society. As a result of the unsolved differences, the U.S. Public Health Service has reportedly held up a five-year $24,000,000 grant award the CRMP seeks to set up shop.

   "The objections of the Medical Society are far from insurmountable. The Society justifiably feels that it should be a strong partner in any health plans for the state and this can be done by appropriate structuring of the advisory board. A policy-making voice should be given to members of the profession who represent private medical practice.

   "Establishment of an harmonious working relationship between the two medical colleges of the state and the Medical Society will yield important results in the cause of medical progress. Once such a satisfactory relationship is accomplished, the result should be a regional medical care network with co-operative effort in research, clinical services, education and other vital elements in the field of medicine."

5. **MEDICARE COSTS.** Beginning January 1, 1969 beneficiaries of hospital care under Part A of Medicare will pay the first $44 instead of $40, which has been the patient's responsibility since Medicare went into effect July 1, 1966. Wilbur J. Cohen, Secretary of HEW, attributed the increase to "the constant rise in hospital costs." Others believe, however, that Medicare costs were underestimated by the administrators first set up the program.

6. **DRUG PROBLEM.** U.S. Senator Gaylord Nelson, D-Wis., has accused the AMA of being "grossly derelict about keeping doctors informed about the accuracy of claims made by drug manufacturers for their products. His statement

was prompted by testimony of Dr. Philip R. Lee, an assistant secretary in HEW that "most of the drug information received by practicing physicians comes from the advertising and promotional activities of drug companies. Sen. Nelson chided the AMA for not screening drug ads in JAMA for factual content.

7. **X-RAY TECHNOLOGY SCHOOL.** The AMA has approved the opening of a school of x-ray technology at Park City Hospital. The two-year program will include instruction in anatomy, physiology, physics, patient care, and x-ray procedures in conjunction with actual practical application within the hospital.
8. **HEALTH CAREERS SCHOLARSHIPS.** The New Haven County Medical Auxiliary has awarded health careers scholarships valued at $1,550 to eight young women. The award winners, all recent high school graduates, are beginning their studies in preparation for careers in the field of health. The Auxiliary has given over $7,000 in health careers scholarships over the last five years.
9. **SALARY INCREASES.** In New York City the salary for interns is going up from $4,500 to $7,500 and $7,750 next July 1; sixth-year residents rise from $6,300 to $10,500 now and $10,750 next July 1. Increased living allowances have also been granted to interns and residents.

"WHAT YOUR STATE DIVISION OF VOCATIONAL REHABILITATION DOES FOR THE DISABLED——."

C. F. Yeager, M.D.

Administrative Medical Consultant, Division of Vocational Rehabilitation, State Department of Education, Hartford, Connecticut. Consultant in Occupational Medicine, Bridgeport Hospital, Bridgeport, Connecticut.

WHAT IS REHABILITATION?

Rehabilitation is a public service established by the State Board of Education in 1929, designed to develop and restore the working usefulness of handicapped individuals to the point where they may become self-supporting.

TO WHOM IS IT AVAILABLE?

Any handicapped person residing in Connecticut who can be reasonably expected to profit by rehabilitation services should apply for consideration. Disabled veterans are eligible to the extent that they are not entitled to or receiving similar benefits through the Veterans Administration.

Persons with disabilities resulting from birth, disease, accident, from emotional or behavioral causes are served. These include, arm and leg deformities, amputations, heart ailments, tuberculosis, hearing, speech and eye defects, mental illness, environmental and many other handicapping conditions.

WHAT SERVICES ARE PROVIDED?

The range of services to disabled individuals includes:

1. Full evaluation, including medical diagnosis, to learn the nature and degree of disability and to help evaluate the individual's work capacities.
2. Counseling and guidance in achieving good vocational adjustment.
3. Medical, surgical, psychiatric, and hospital care and related therapy, to reduce or remove the disability.
4. Artifiicial limbs and other prosthetic and orthotic devices needed to increase work ability.
5. Training, including training for a vocation, prevocational and personal adjustment training, and remedial education.
6. Service in comprehensive or specialized rehabilitation facilities, including sheltered workshops and adjustment centers.
7. Maintenance and transportation when necessary for the disabled person to derive the full benefit of other vocational rehabilitation services.
8. Tools, equipment, and licenses for work on a job or in establishing a small business.
9. Placement in a job suited to the individual's highest physical and mental capacities.
10. Post-placement follow-up to see to it that the placement is satisfactory to the employee and the employer.

HOW DO THE DISABLED BENEFIT?

Services are provided to meet the individual needs of disabled persons so that they may engage in safe and suitable occupations or, to determine that the individual will benefit from such a program of rehabilitation services. Such services are provided at public expense.

Many physical or mental handicaps can be removed through vocational rehabilitation services. Others may be corrected to the point where they do not interfere with work demands or properly selected jobs. Employment records of thousands of vocationally handicapped persons have proved that:

It's not what a man has lost, but what he has left that's important.

HOW ARE SERVICES SECURED?

Apply at any one of the
following offices

STATE OFFICE

Division of Vocational Rehabilitation
Connecticut State Department
of
Education
Shelbourne Building
600 Asylum Avenue
Hartford, Connecticut 06105
Tel. 527-6341, EXT. 3336

DISTRICT OFFICES

Address	Zip Code	Phone
BRIDGEPORT		
575 Broad Street	06604	336-1835
HARTFORD		
122 Washington Street	06106	278-7810
NEW HAVEN		
1 State Street	06510	787-1277
NORWICH		
257 Main Street	06360	887-3546
WATERBURY		
8 Prospect Street	06702	757-1581

LOCAL OFFICES

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1001 Farmington Avenue	06010	584-2413
DANBURY		
95 Locust Avenue	06810	748-4154
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PUTNAM		
168 Main Street	06260	
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26 Palmer's Hill Road	06902	325-1544
TORRINGTON		
122 Water Street	06790	482-2495

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Dear Doctor. Edited by Juliet Lowell. Funk & Wagnalls, New York, 1968. 179 pp. Illustrated. $3.95.

Today's Health Guide, Revised Edition. Published by the American Medical Association, 1968. Edited by W. W. Bauer, M.D. 624 pp. $5.00.

Infectious Diseases Of Children. Fourth Edition. Edited by Saul Krugman, M.D. and Robert Ward, M.D. The C. V. Mosby Company, Saint Louis, 1968. 428 pp. $16.50.

The Country Doctor And The Specialist. Edited by Fred Lyman Adair, M.D. Adair Award Fund, Box 65, Maitland, Florida, 32751, 1968. 215 pp.

Nutrition And Infection. Ciba Foundation Study Group No. 31. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1967. 151 pp. 20 illustrations. $3.50.

Decision Making in National Science Policy. A Ciba Foundation Symposium. Edited by Anthony De Reuck, Maurice Goldsmith and Julie Knight. Little, Brown and Company, Boston, 1968. 310 pp. Illustrated. $12.00.

Interferon. Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1968. 271 pp. Illustrated. $12.00.

Anesthesia For Infants And Children, 3rd Edition. Edited by Robert M. Smith, M.D. The C. V. Mosby Company, Saint Louis, 1968. 530 pp. with 240 illustrations. $17.50.

Pediatric Therapy, 3rd Edition. Edited by Harry C. Shirkey, M.D. The C. V. Mosby Company, Saint Louis, 1968. 1294 pp. with 351 illustrations, $25.00.

Evaluation of Results of Cardiac Surgery. American Heart Association Monograph Number 22. Edited by Lewis Dexter, M.D. and Lars Werkö, M.D. American Heart Association, Inc., 44 East 23rd Street, New York, N.Y. 10010. 112 pp. $4.00.

Life Or Deaths Ethics And Options. Edited by Daniel H. Labby. University of Washington Press, Seattle, 1968. 167 pp. $4.95.

Principles of Applied Biomedical Instrumentation. Edited by L. A. Geddes and L. E. Baker. John Wiley & Sons, Inc., New York, London and Sydney, 1968. 479 pp. $13.50.

Hypertension, Volume XVI. Neural Control of Arterial Pressure. Edited by J. Edwin Wood, M.D. The American Heart Association, Inc., 44 East 23rd Street, New York, N.Y., 10010, 1968. 119 pp. $3.00.

Spare-Part Surgery: The Surgical Practice of the Future. Edited by Donald Longmore. Doubleday Science Series, Doubleday & Company, Inc., Garden City, New York, 1968. 192 pp. $5.95.

Medical Pharmacology: Principles and Concepts, 4th Edition. Edited by Andres Goth. M.D. The C. V. Mosby Company, Saint Louis, 1968 749 pp. $13.50.

WOMAN'S AUXILIARY

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The 25th annual conference of state presidents, presidents-elect, national officers and chairmen of the Woman's Auxiliary to the American Medical Association, Inc., was held in Chicago, Illinois, September 29th through October 2nd.

Home-centered health care, use and abuse of alcohol and drugs by today's youth, AMA-ERF, speaker's seminars, medical manpower, legislation, Ship HOPE, and health careers were among the subjects discussed at the conference which attracted approximately 175 auxiliary leaders.

From the list of subjects discussed it is obvious that each day was filled with information to be noted and filed for future reference. The purposes of the conference are to inform the two top officers of each state of programs now underway, of programs to be stressed in the future, and to teach them how to improve themselves to be better able to further auxiliary work.

Previously, this column has discussed the package programs available for auxiliaries to present. The question arose as to whether another organization might sponsor one of these programs. It was decided that this might be done, but an auxiliary member would have to be present and involved in the presentation of the program.

Joseph B. Trainer, M.D., of the University of Oregon Medical School and author of "Human Mating and Marriage" informed and entertained the women with his talk "Special Characteristics of the Physician's Family". He offered the following suggestion for the doctor's wife: "Give your first priority to the cultivation of your own personal relationship, recognizing that with the first priority will go only a minuscule amount of true time. You came together because some things in your mutual personalities were individually attractive. Try to keep them. Both males and females bring into the relation some common human characteristics, and each needs to fill this for the other. Each must, if they are to be truly successful, meet the need of the other for attention, approval, and love and affection. Each must be the guardian of the dignity and the privacy of the other. Each must secure to the other the avoidance of loneliness.

"The Use and Abuse of Alcohol and Drugs by Today's Youth" was discussed by Herbert A. Raskin, M.D. of Wayne State University, Detroit, Michigan. Dr. Raskin emphasized again that there is no such thing as a safe drug and explained about the proper use and abuse of drugs. He said we must work against the abuse by an unknowing person who is not informed as to the possible side effect. Teens especially need to learn to develop inner resources to stand the pressures of the world, and if they reach for something outside themselves like drugs for help, the drugs take the place of the strengths which are never developed.

At the Monday luncheon Dwight L. Wilbur, M.D., president, A.M.A., was the guest speaker. He reminded the auxiliary of its influential position in guiding youth into health careers, and emphasized that escalation is important in health careers when in a few years one out of every seven high school graduate should go into the health field. He can see very little chance that the auxiliary will ever run out of things to do in the medical manpower field.

The Monday session ended with dinner sponsored by AMPAC. Guest speaker for the event was Shirley Temple Black, who discussed her recent trip to Europe on behalf of the Multiple Sclerosis Foundation, and especially her trip to Prague and her escape from Czechoslovakia under the Russian guns. She encouraged the women to become more involved in politics and to listen to the candidates and what they say.

The Tuesday, October 1 meeting began with the AMA Seminar on Public Speaking. Roy Wood, Ph.D., associate dean, School of Speech, Northwestern University, presented guidelines for methods of self improvement. Mr. Mortimer Enright and Mr. Edward Uzemack of the AMA staff joined with Dr. Wood to present a panel discussion on the art of public speaking. Some members of the auxiliary volunteered to participate in a manuscript reading drill and the preparation of a three minute speech trying to use the techniques discussed by the panel.

Mrs. Herbert L. Mantz, parliamentarian, gave tips on "So You Are Going to Have a Meeting" which should help the auxiliary to hold better organized meetings by having a knowledgeable president.

The duties of the legislative chairmen were outlined briefly Further work to be done in health careers, including studies of communities and their needs, plus retraining for inactive nurses was discussed.

A representative of the Pharmaceutical Manufacturers Association discussed the prescribing of drugs by generic name and their stand on the matter.

On Wednesday, October 2, a tour of AMA headquarters began the session. The remainder of the morning was devoted to a film presentation in the AMA's 9th floor auditorium. "To a Baby-Sitter" from the GEMS program and a color film "Marihuana" were shown.

Following the showing of the films the conference was ended, those attending to return to their home states better prepared to carry out the duties required of them in the days ahead.

MEETINGS

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospitals Auditorium, New London

November 5 7:15 P.M.

The Rational Treatment of Chronic Renal Failure

Speaker: Donald E. Oken, M.D., Associate Director, Cardiorenal Laboratory, Peter Bent Brigham Hospital

November 19 7:15 P.M.

Renal Transplantation

Speaker: John P. Merrill, M.D., Senior Associate in Medicine, Peter Bent Brigham Hospital; Associate Clinical Professor of Medicine, Harvard Medical School.

MEDICINE

November 6 9:30 A.M.-4:30 P.M.

Annual Meeting of Connecticut Thoracic Society, Medical Section of the Connecticut Tuberculosis and Respiratory Disease Association

Connecticut Mental Health Center Auditorium, 34 Park Street, New Haven

Program: Welcome, Harold Stern, M.D., CTS President; Moderator, Lyndon E. Lee, Jr., M.D., Director of Surgical Service and Chief of Extra Veterans Administration Research, Washington, D.C. Panel, "Survival Factors in Lung Carcinoma," John Steele, M.D., Chief of Surgical Service, San Fernando VA Hospital; George A. Higgins, M.D., Chief of Surgical Service, Washington, D.C., VA Hospital; Julius Wolf, M.D., Chief of Medical Service, Bronx, N.Y., VA Hospital; Raymond Yesner, M.D., Chief of Pathology Service, West Haven VA Hospital. Case histories of "Newer Modalities in Diagnosis and Treatment of Lung Cancer," Joseph P. Dineen, M.D., Clarence E. Cahow, M.D., Assistant Professors of Surgery, Yale Medical School. Discussion, "Preoperative Irradiation of Lung Cancer." John T. Mallams, M.D., Professor of Radiology, Yale Medical School.

Contact: Jon H. Harrison, 634 Asylum Avenue, Hartford, Phone: 527-9206

November 13 All Day

Connecticut Conference on Alcohol Problems

Holiday Inn, Meriden

Participants: Stanley E. Gitlow, M.D., New York Medical College; Ernest A. Shepard, Chief, Alcohol and Drug Dependence Division, State Department of Mental Health; John D. Carney, District Director of Education, United Steel Workers of America; Francis Keefe, Production Planning Manager, Fenn Manufacturing Co.; Richard J. Tatham, Chief, Office of Alcoholism and Drug Addiction Program Development, Washington, D.C.; the Rev. David Workers, Executive Vice-President, North Conway Institute; Mrs. Marty Mann, Founder-Consultant, National Council on Alcoholism, New York.

November 15 9:00 A.M.-5:00 P.M.

Symposium on Perinatal Mortality

Connecticut General Life Insurance Company Building, 900 Cottage Grove Road, Bloomfield

Sponsored by the Committee on Perinatal Mortality, Connecticut State Medical Society; Connecticut State Health Department, Yale University School of Medicine.

Participants: Moderator, Mary Ellen Avery, M.D., Associate Professor of Pediatrics, John Hopkins Hospital, Baltimore; Guest Lecturers, John W. Greene Jr., M.D., Lexington, Kentucky; Kurt Hirschorn, M.D., Professor of Pediatrics, Mt. Sinai, School of Medicine, New York City; Fritz Fuchs, M.D., Professor of Obstetrics and Gynecology, Cornell University Medical School, New York City; Louis Gluck, M.D., Professor of Pediatrics, University of Miami School of Medicine; Philip Sarrel, M.D., U.S. Army, while at Yale University, Director of the Unwed Mothers Program; Bradley E. Smith, M.D., Associate Professor of Anesthesiology, University of Miami School of Medicine; and Milton Markowitz M.D., Associate Professor of Pediatrics, John Hopkins Hospital, and Professor-Chairman of Department of Pediatrics, University of Connecticut Medical School, Beginning July 1, 1969.

Luncheon available on premises.

PSYCHIATRY

November 13 **1:30 P.M.**

Personality Development and Psychopathology

Kettle Building, Norwich Hospital

Sponsor: Connecticut Postgraduate Seminar

Speaker: Maurice E. Linden, M.D., Director, Experimental and Demonstrational Mental Health Service, Philadelphia State Hospital.

Contact: Vincenzo Socilovo, M.D., Assistant Superintendent, Norwich Hospital. Phone 889-7361, Ext. 264

Seminars sponsored by the Connecticut Valley Hospital, held in Merritt Hall Auditorium

November 21 **10:30 A.M.**

"Witchcraft and Culture Psychiatry," George Mora, M.D.

December 3 **10:30 A.M.**

"The Double Life of the American Psychiatrist," Henry A. Davidson, M.D.

December 10

"Abortion, Euthanasia, and the Psychiatrist," Jay Katz, M.D.

December 9 **2:30 P.M.**

"Ego and the Hypnotic State," Harold Rosen, M.D., Ph.D.

Tuberculosis? Influenza?
Pneumonia? Leukemia?
Hodgkin's Disease? Syphilis?
Systemic Fungal Diseases?
Chronic Chest Diseases?
or

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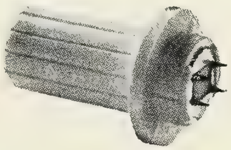
(Histoplasmosis—"The Masquerader")



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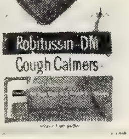

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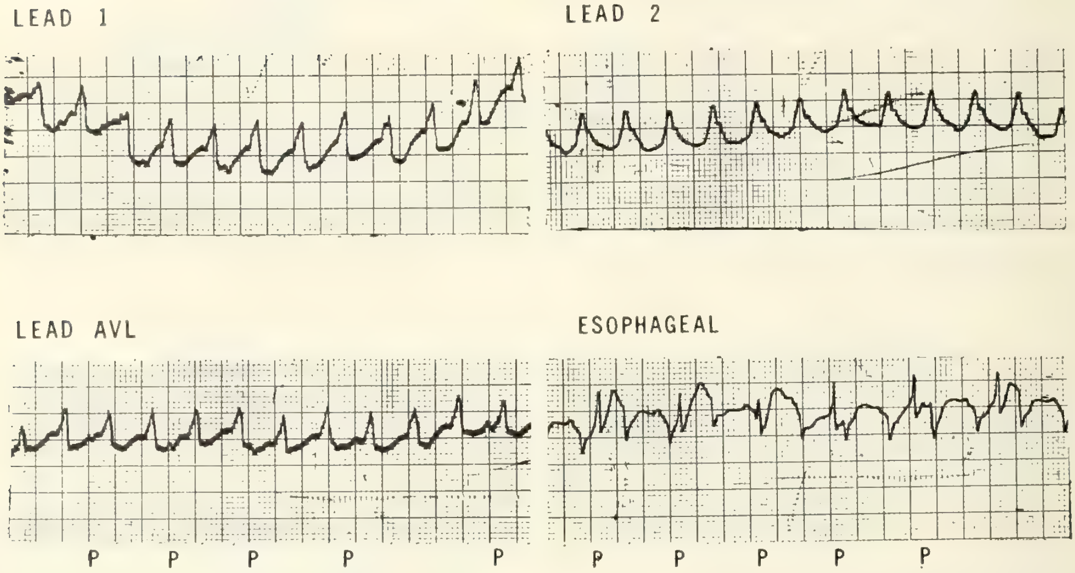
A-H-ROBINS

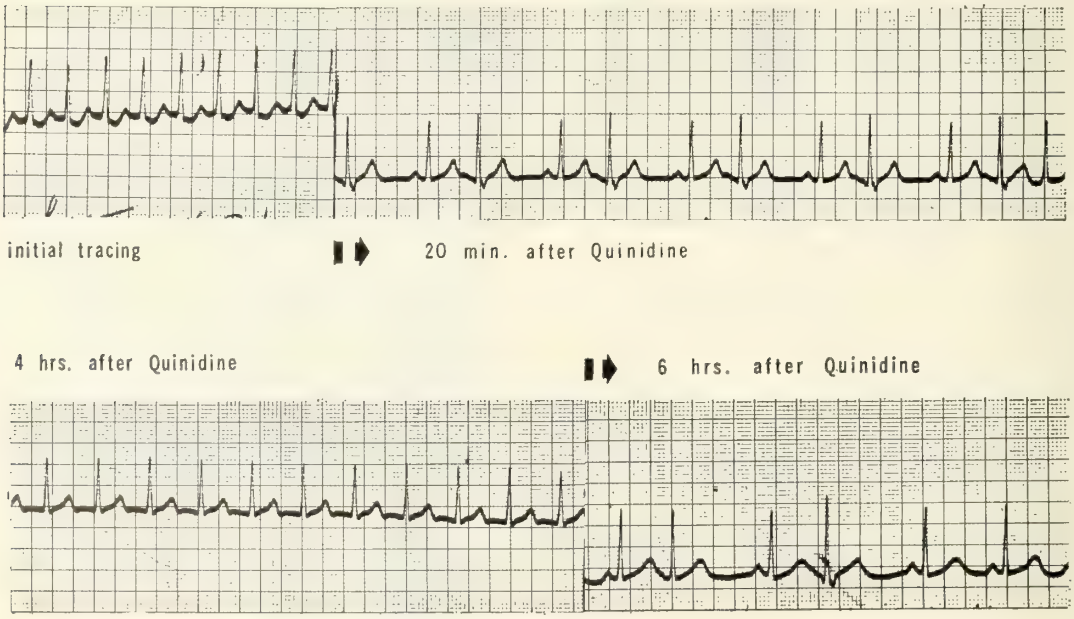
Electrocardiograms of the Month

Montefiore Hospital and Medical Center
The Bronx, New York

Editors
IRA L. RUBIN, M.D.
Head, Department of Electrocardiography
JULIAN FRIEDEN, M.D.
Associate Head, Department of Electrocardiography



QUESTION 1. What is the arrhythmia as seen in leads I and II? The patient is a sixty-four-year-old male with bronchopneumonia.



QUESTION 2. What is the rhythm in each of the four strips?

Electrocardiograms of Month

ELUCIDATION

Question 1. There is aberrant conduction of the regular ventricular beats at a rate of 166. The QRS duration is 0.12 seconds. The differential diagnosis is either a supraventricular tachycardia with aberrant conduction or ventricular tachycardia. The diagnosis is established by the identification of P waves (atrial activity). In lead a VI, the P waves may be seen beating at a rate of 100 and independent of the ventricular beats. This is further proved with an esophageal lead which demonstrates large P waves. Careful examination of lead I also reveals the diagnosis; clearly demonstrable P waves follow the third, fifth, and seventh ventricular complexes.

In lead II, atrial activity is not identifiable. When a rapid ventricular rate is present with a prolongation of the QRS of greater than 0.12 seconds, one must differentiate supraventricular from ventricular tachycardia. A careful search must be made for P waves in each lead. Exploratory leads such as bipolar chest leads, esophageal leads, or right atrial leads may be necessary. The diagnosis of ventricular tachycardia is justified only when the atrial rate is independent of, and slower than, the ventricular rate. Further confirmatory evidence such as fusion and capture beats may be present in some electrocardiograms.

Question 2. The initial record is a paroxysmal supraventricular tachycardia at a rate of 166. No P waves are visible. Following the initial record, 0.4 Gm. of quinidine was given to this patient intramuscularly. Twenty minutes later the rhythm had converted to a sinus rhythm with bigeminy due to atrial premature beats which are aberrantly conducted. Note the P wave preceding each of these beats. Four hours after quinidine, the supraventricular tachycardia recurred at a slower rate of 125. At this time, the P waves are again buried in the preceding T wave. Six hours after a second dose of quinidine, 0.4 Gm. intramuscularly, sinus rhythm with premature atrial beats, some aberrantly conducted, has been restored with a longer Q-T interval.

These tracings illustrate several of the actions of quinidine. (1) It converts paroxysmal supraventricular tachycardia to regular sinus rhythm. (2) The recurrent supraventricular tachycardia was at a slower rate, because of the quinidine effect of deceasing automaticity of the ectopic focus. (3) Quinidine prolongs electrical systole, as indicated in the final record by the prolongation of the Q-T interval.

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Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

Louis H. Nahum, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

Connecticut Medicine

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Manuscripts, including references or bibliography, must be typewritten, double-spaced on white paper 8½ x 11 inches with adequate margins on firm paper. The original copy, not the carbon copy should be submitted. Carbon copies or single spaced manuscripts will not be considered. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Receipt of manuscripts will be acknowledged and unused manuscripts returned. *Accepted* manuscripts become the permanent property of the Journal and may not be reprinted elsewhere without permission from both the author and Connecticut Medicine. The author is responsible for all statements made in his work, including changes made by the copy editor.

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The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the Journal (listing name and initials of author, title of article, journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

ILLUSTRATIONS

Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration as well as typed on a separate sheet. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. Connnecticut Medicine will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

NEWS

Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

ADVERTISING

All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by Connecticut Medicine.

Material other than original articles should be received not later than the 10th of the month PRECEDING date of issue.

REPRINTS

Reprint orders should be returned at once as the type will be destroyed immediately following publication of the manuscript. The Journal does not stock reprints of the articles published. Requests for individual reprints should be sent to the author.

Communications should be addressed to Connecticut Medicine, 160 St. Ronan Street, New Haven, Conn., 06511 Telephone 865-0587.

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Connecticut Medicine

Connecticut State
Medical Journal

Volume 32/December 1968/Number 12

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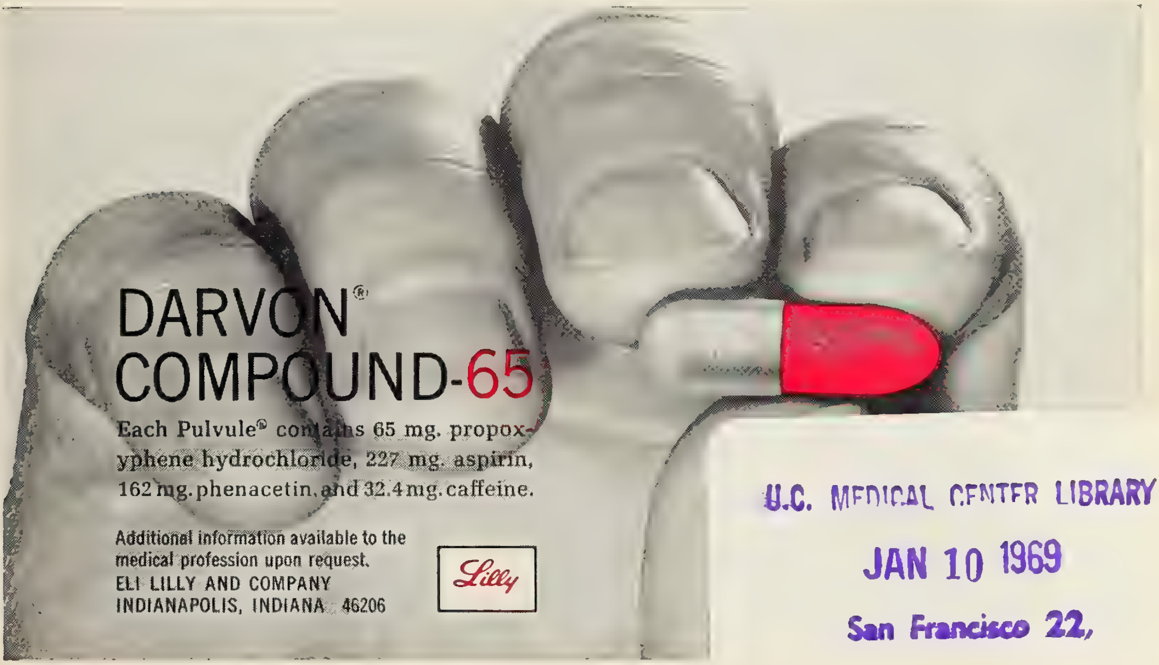
Courtesy Ned Thomas, science-medical reporter, The New Haven Register



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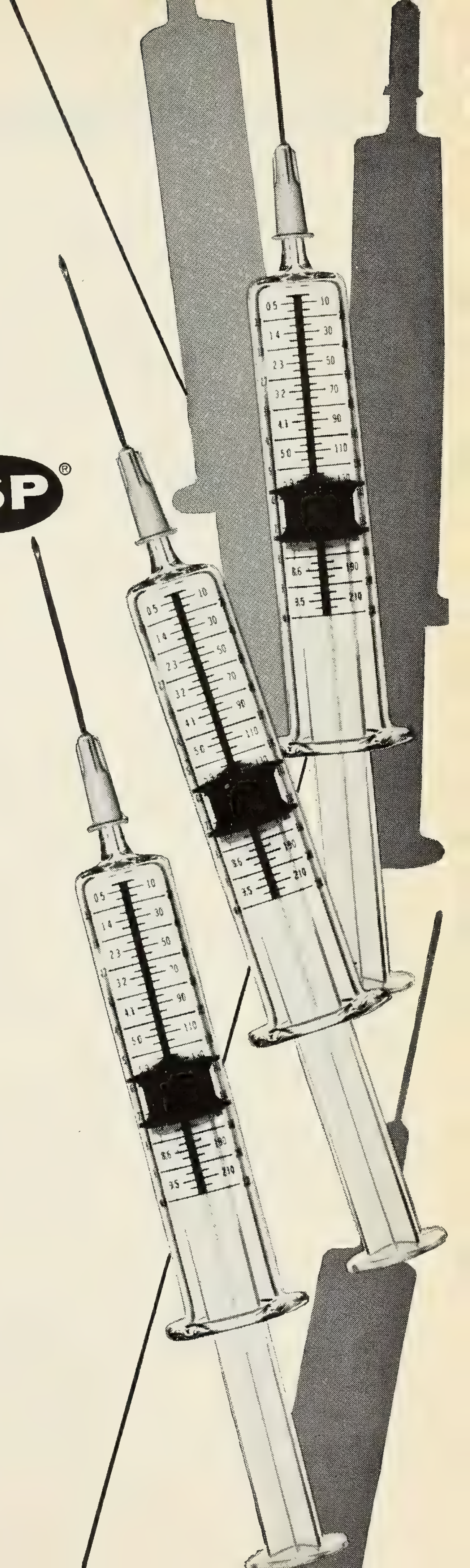

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Connecticut Medicine

DECEMBER, 1968
Vol. 32/No. 12

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Connecticut Medicine

editorials

Air Pollution:
II. General Preventive Principles

On February 29, 1968, the late Senator Robert F. Kennedy said that if present air pollution trends continue, New York City will be uninhabitable within twenty years. "The unchecked waste which fouls our air each day makes the very act of breathing a menace to our health." The preventive principles to consider of this hazard arise from the well established fact of the relationship between the quantity of pollutants and the extent of the biological effects they are likely to produce. To combat the dangers of pollution we must try to reduce as much as possible the chemical pollutants of the air. A whole range of measures of a technical nature can be taken to this end.

One, is siting properly the sources of pollution. The separate zoning of industries causing pollution and residential areas is of paramount importance. To achieve this separation, we need to have in addition to decentralization, well thought out town and country planning which allows for the creation of green wooded belts separating residential areas from centers of pollution. Another urgent requirement is a reduction of the amounts of pollutants produced by the various sources listed above.[1]

Recommended methods of achieving this include concentrating the centers of pollution as much as possible and away from towns. This means also that an extension of town heating should be encouraged. There is needed also adjustment and supervision of fires, the setting of standards for the fuels used, covering in particular their sulphur content. Important is purification of smoke and effluent from factories before they are released into the atmosphere (at a suitable height above ground level). Last but not least is the perfecting of devices for fitting motor vehicle enginees which will cut the amount of pollutants in the exhaust gas to a minimum, acting either before the combustion chamber or after it (by using a system of purification).

We should impose very stringent controls on the way vehicle engines, especially diesel engines are adjusted. One needs walk along ring roads or follow buses and trucks to see that most diesel engines are badly adjusted and pour out clouds of thick black smoke from their exhaust pipes. The police would not need to have any special knowledge of chemistry to be able to recognize an infringement of this kind and it would only need a vehicle to be put off the road a couple of times because of a badly adjusted engine for sufficient losses incurred to encourage the owner to make sure that the burners are always properly set.

The effectiveness of the preventive measures outlined above is confirmed by the comparative analysis of air over two industrial towns in Siberia. Irkutsk is dotted by factories throughout the city and houses are heated by small coal burning stoves. Over this town the air contains a high level of benzpyrene. Nearby Irkutsk is Angarsk with town central heating and factories separated from the rest of the town by a strip of forest one mile wide. Over Angarsk there are no more than slight traces of benzpyrene.[1]

Naturally any preventive measures against air pollution must be accompanied by supervision. Furthermore the public at large must be made aware of the dangers and the urgent need to overcome them. One of the most important forms that this takes is a regular check on the purity of the air we breathe and this requires suitable methods of its analysis. Here we need to set up permissible limits of concentration of the various potentially poisonous substances. Truhaut has studied this question in detail as has the Committee of Experts of WHO.[2] These have emphasized two points of outstanding importance. The permissible limits to be adopted for the air over cities must be a good

ABOUT THE COVER

A dense, black column of smoke billows skyward from one of the auto graveyards along Middletown Avenue, New Haven, as old automobiles burn, throwing particulate matter, hydrocarbons and noxious gases into the air.

deal lower than those relating to occupational exposure.

The general public we must remember is exposed twenty-four hours a day, workers only seven to eight hours, five days a week which allows more chance for recuperation. Adult workers mostly undergo initial examinations and periodic checks. This makes it possible to exclude those in poor physical condition. The general public includes infants, children, old people, expectant mothers, invalids and persons suffering from organic deficiencies or hidden complaints, all of whom may be more vulnerable to poisons in polluted air than ordinary adults. To put this situation (not usually appreciated) into concrete form there is the example of beryllium which is permitted in work places at 2 gammagrams/m^3 while that for air breathed by the public at large is 200 times lower at .01 gammagram/m^3.

Our knowledge of the toxicity threshold of chemical pollutants found in the air over cities and industrial environments is still in the majority of cases in an embryonic stage. We are particularly vague as to the insidious long term effects on the health of populations exposed to polluted air. This lack of certainty is all the more disquieting to toxicologists and Public Health authorities since certain pollutant substances have been found to be definitely harmful even in minute quantities. This has at least in a number of countries led the authorities to impose regulations aimed at reducing the emission of these substances such as the Clean Air Act in Great Britain and the French Law on Pollution of the Atmosphere.

Air pollution is now recognized as a real social scourge on a world-wide scale because of the often insidious hazard to health that it represents. It is incumbent on the government as a matter of urgency to encourage and assist experimental research and epidemiologic surveys which will give the measure of these health risks. This is an essential precondition to setting up standard measures in collaboration with the other disciplines involved and, of course, soberly without wildly over or understimating the economic and social aspects of the problem.

Measures to protect the health of the public is an urgent responsibility of government, for the public in general unfortunately is unable to choose what air it breathes. Senator Kennedy and Senator Jacob K. Javits urged a Senate subcommittee to give quick approval to a proposed five-state compact aimed at controlling air pollution in the Middle Atlantic Region. The proposed compact would establish a commission with power to enforce standards of air cleanliness. The compact has already been endorsed by Legislatures of New York, New Jersey and Connecticut. Once the compact is brought into effect we the public must remain vigilant that the enforcement does not fall into the hands of the polluters. We can feel confident that the Department of Health will remain good guardians of the health of the people and able watch-dogs for the correct enforcement of such a compact.

L.H.N.

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Drafts, Cold and Colds

As far as experimental bacterial, rickettsial and viral infections in animals is concerned it is well established that exposure to cold may dramatically increase the frequency and severity of illness. In man, however, limited studies have demonstrated no effect of exposure to cold on susceptibility to infection with the common cold viruses. Now Douglas et al[1] have provided further significant negative evidence on the long-asked question of what is the effect of exposure to cold on the common cold. They chose to use for the test rhinovirus type 15, a representative of a group of agents most frequently the cause of the common cold. They exposed subjects in a 4° C. room and a 32° C. water bath and gave them measured doses of virus. The subjects were exposed at selected intervals: at inoculation, during incubation, during the maximum illness and during recovery. They made observations on infectivity, illness severity, quantitative virus-shedding patterns, antibody response, and leucocyte response and bacteriologic flora of the upper respiratory tract, in subjects exposed to colds and in a similar number of controls. Exposure to cold did abolish the characteristic increase in neutrophils during illness. There were no significant changes in the other findings between subjects exposed to rhinovirus type 15 and cold and those exposed to virus alone. Clearly the host resistance was not affected by cold exposure.

There are at least three possible explanations for the "no effect" of cold on the common cold.

There is no effect of environmental temperature on the common cold: exposure to cold for longer periods or to more severe conditions may be necessary to influence the course of rhinovirus common colds: exposure to cold influences the course of other viral illness in man even though it does not affect rhinovirus illness. Other host factors such as age, sex, fatigue, exercise and the time of day the inoculation took place which might be associated with chilling in nature were of course not tested.

If the results obtained with a single strain of virus are accepted as indicating generally that cold exposure has no effect on susceptibility to the common cold how then do we explain the general notion that drafts cause colds and how do we explain in the temperate zones of the peak incidence of colds in the winter and early spring. One explanation of an effect of cold and drafts that immediately comes to mind is that the chilly sensations that usually mark the onset of a cold have been misinterpreted as a causative factor in the illness when, in fact, it was merely a coincidence because cold weather and colds usually go together.

Numerous experiments reveal that in a large percentage of susceptible volunteers quartered in warm rooms and inoculated with an infectious dose of any of several common-cold viruses, a cold will develop. The now classic study on the island of Spitzbergen by Paul and Freese[2] in 1933 revealed that when the islanders were isolated during the winter season, at a time when exposure to cold occurred regularly, colds almost disappeared but promptly reappeared in epidemics during the spring on return of the ships. Their viral inoculation in the absence of exposure to cold resulted in a cold, but colds did not occur in a cold climate in the absence of a source of viral transmission.

In Panama[3] an increased frequency of colds occur at the start of the rainy season while a low frequency of such illnesses is observed in the dry season. The annual mean temperature was 80° F. and fluctuations did not exceed 5° F. Monto and Johnson accordingly suggested that the increase in colds with the onset of the rainy season may have resulted from closer contact among the inhabitants who spent more time indoors because of the rain. As in Spitzbergen it was opportunity for transmission of virus rather than environmental causes that led to outbreak of colds.

Lidwell et al[4] recently analyzed nine weather variables such as westerly weather, sunshine, rain and humidity in relation to occurrence of common colds in study populations in London and Newcastle. They did find an association of sufficient magnitude to account for the greater part of the seasonal variation in the incidence of colds. The authors suggested that low outside temperatures promote transmission of the virus or the development of the disease. If outside cold appears then two to four days later colds appear. Douglas' failure to show a significant effect of exposure to cold on rhinovirus cold at the time of inoculation (2-4 days before the onset of illness) and at other times makes it highly improbable that temperatures themselves have a direct effect on development of colds.

There is an alternative explanation namely that cold weather like rain in the tropics keeps people indoors more of the time creating more opportunities for transmission of virus. Certainly the work of Douglas and his colleagues serve to de-emphasize the age old concept of an effect of cold on the common cold. If dissemination of virus during cold weather and rainy weather accounts for the increased frequency of colds our attention must now be directed to a study of the indoor environment and how reduced transmission of virus may be accomplished.

L.H.N.

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The College Of Human Medicine Michigan State University

Michigan State University's College of Human Medicine has now admitted two classes of twenty-six students each and now has a third class this fall. Each class is a pilot group pioneering new approaches to medical education. Although officially classified as a "two year" medical school, the college actually offers a three year program. The students are admitted in their fourth college year when they take the usual first year medical school courses such as anatomy, physiology and biochemistry but with one-third fewer content hours than

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average. Added by MSU is a special year-long seminar in "Medicine and Society" designed to give students a better understanding of the broad context of health care. In teaching this seminar a wide range of teaching talent are recruited from throughout the university and community including anthropologists, psychologists, sociologists and social workers as well as physicians.

The next year the curriculum is the human biology sequence. This is a core program which focuses on the growth and development of the human being from conception to senescence. Taking part in the instructional program are faculty from a wide range of biological and behavioral disciplines. The students are introduced to clinical experience at the beginning of this year. Their first contact is with "simulated patients," actors and actresses who have been "programmed" to portray specific sets of symptoms and personality characteristics during interviews with medical students. The primary aim is to help medical students to be sensitive to the individual patient. Each interview is viewed live on closed circuit television by the instructor and other students and then played back to the interviewer and the class. There follows a critique which is of benefit to all. All of the simulated patients were programmed differently but each case dealt with pregnancy or the reproductive process in line with the subject matter at the beginning of the human biology sequence.

Following this introduction students in the human biology sequence soon gain additional patient experience at the university health center, local hospitals and other community agencies. Initial experiences begin with pregnancy and delivery and then progress to the newborn and young children. The third year studies in clinical experiences will deal with the health of the adolescent and the adult. Throughout the curriculum, the emphasis is put on self-study and students are encouraged at every opportunity to learn for their own good and not simply for the sake of making a better grade. The expectation is that self-learning will create habits of lifelong study of medicine as it grows and changes.

There is a close integration of the College of Medicine in the administrative structure of the whole university. This enables the college to both draw upon and contribute to the total resources of the university through the Institute of Biology and Medicine which is part of the Office of Provost and is responsible for overall coordination and integration of the health program. This concern for integration also led to the joint administration of several basic science departments by the College of Human Medicine, the College of Veterinary Medicine, the College of Natural Science, the College of Social Science and the College of Agriculture.

For example the Department of Microbiology which was formerly administered by the Colleges of Natural Science and Veterinary Medicine now is being administered in addition by the College of Human Medicine. This type of joint administration will lead to a number of cooperative interdisciplinary programs. Besides the usual departments of anatomy, physiology, pharmacology, biochemistry and biophysics, the College of Human Medicine has also a Department of Zoology, and three behavioral science departments, anthropology, psychology, and sociology. Complementing these departments are three clinical departments, medicine, human development (responsible for the human biology sequence in the second year) and psychiatry. Other units are the Office of Medical Education Research and Development and a School of Medical Technology.

The Office of Medical Education Research and Development will conduct ongoing and long-range evaluations of the program. In addition to more formal programs of evaluation this office encourages and aids educational innovation and evaluation on the part of the faculty who are now willing to try new approaches to medical education and then carefully evaluate what has been done. Such an attitude doubtless will lead to a continuing propensity for innovation.

Looking ahead, the class size will be enlarged to sixty-four students as soon as the proposed Life Sciences Building is completed perhaps by the fall of 1970. This $10 million building will then house the Department of Medicine, the Department of Pharmacology and the School of Nursing. Of course, a clinical science building and a teaching hospital—outpatient center are considered necessary for a full program, even though extensive use will presently be made of community hospitals and other resources. For the small number of students in the first classes, however, it may be possible to use community facilities to give students the kind of clinical experience required for the M.D. degree.

The College of Human Medicine in M.S.U. is in a unique opportunity to lead the way towards a new form of medical education. Everyone now recognizes the greater sophistication and preparation of medical students entering medical school as compared with several decades ago when the classical curriculum was formalized in response to the Flexner report of 1910. There is now marked heterogeneity in interests and career objectives of students. Students appear to desire early patient contact. There is a growing involvement of students and faculty in the social and community aspects of medicine. In the older schools much dissatisfaction has developed among both students and developed among both students and faculty alike with inflexible and frequently repetitious courses of excessive length and minimal importance to some students who have special career objectives.

The College of Human Medicine in M.S.U. has recognized the need for interdepartmental coordination and for a built in system for ongoing and long-range research that will continue to evaluate the results of their experiment in medical education. From now on the static nature of curriculum and learning will give way to continuing search for new forms.

L.H.N.

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Sex-Control And The "Health" Of Society

Experiments are now underway to control sex of the newborn infant. The success so far is on frogs and rabbits while on human sperm it is still quite limited and even when spermatozoa can be separated, the XX from the XY, it will still be necessary to employ artificial insemination. The question that must be met is what might be the societal consequences of sex control. Furthermore, if they should on balance be undesirable then can sex control be prevented without at the same time curbing free scientific inquiry. Are there any circumstances under which societal well-being justifies diverting technological developments of basic science research in sex-control. The fact is also that these questions apply to many other areas of scientific inquiry such as work on a biological code, the experimental use of behavior, and thoughtmodifying drugs. Sex-control like all knowledge consists of basic science search for truths and then technological developments for practical ends.

At present although success seems still fairly remote, it is possible by electrophoresis to separate the two kinds of male sperm and the husband's own sperm could be used for insemination with the desired kind of sperm. If drugs taken orally can ultimately be developed then sex-control would be much less expensive, much less emotionally objectionable and probably widely used. It may be expected that by the year 2000 one of the technical innovations will be the capability to choose the sex of the unborn child.

Many couples do have preferences on whether they want boys or girls. In many cultures boys provides an economic advantage as workers or a form of old age insurance. Girls in many cultures are a liability. A dowry must be provided to marry them off; think of a family with five girls. As against this we find some cultures in which girls are profitably sold off. If more couples preferred boys, then what would be the societal consequences. One is that overproduction of boys would increase the value of girls and hence increase their production until a balance is reached. However, this can hardly be relied upon. Mothers prefer boys as a substitute for their own fathers, out of search for security, or Freudian considerations. Fathers prefer boys because boys can more readily achieve success in our society. This appears not to be so in the communist countries.

If, however, there did develop a relative imbalance with a male surplus it might be cumulative. Most forms of social behavior are sex correlated, and sex composition are very likely to affect most aspects of social life. For example women read more books,[1] see more plays, consume more culture than men in this country. Women are typically charged with the moral education of children. Males by contrast account for a much higher proportion of crimes than females. A significant and cumulative male surplus will thus produce a society with some of the rougher features of a frontier town. Furthermore, the diminution of the number of agents of moral education and the increase in the number of criminals would accentuate already existing tendencies which point in these directions thus magnifying social problems which are already overburdening our society.

Some lower classes and minorities specifically seem to be more male oriented than the rest of society and this is likely to intensify interracial and interclass tensions. The extra boys will seek girls in higher status groups or in some other religion than their own in which girls would also be scarce. Other forms of imbalance which cannot be predicted are to be expected. Greenberg states "all social life is affected by the proportion of the

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sexes. Wherever there exists a considerable predominance of one sex over the other in point of numbers there is less prospect of a well-ordered social life. Unbalanced numbers inexorably produce unbalanced behavior.[2]

When asked what would be expected to happen if sex-control were available on a mass basis, Davis, the well known demographer stated that some delay in the age of marriage of the male, some rise in prostitution and homosexuality and some increase in the number of males who will never marry are likely to result. This position is supported from an informal examination of the situation in the USSR and Germany after World War II.[1]

The sex-control problem is only one example of the effects of science on society. There are more dramatic ones. For example the discovery and use of penicillin,[3] the invention of new psychedelic drugs whose damage to the genetic machinery will become evident much later, drugs like thalidomide that cripple the fetus, even attempts at birth control by intrauterine devices which by their irritation might produce cancer, long range effects of pesticides, cancer producing potential of live virus vaccines and many many others. Even a minimum sex imbalance then will produce unmatable mates, add unhappiness to many who will have to avail themselves of prostitution, homosexuality or be condemned to enforced bachelorhood. These are not abstract problems for someone who is desperate to be married but cannot find a mate.

We already recognize some rights of human "guinea pigs." Their safety and their privacy are not to be violated even at the penalty of delaying the progress of science. The rest of society who are not subjects of research and who are as much affected as those in the laboratory have thus far been accorded fewer rights. Theoretically new knowledge, the basis of new devices and drugs are not supposed to leave the inner circle of science before it is safely tested on animals and volunteers and in some instances approved by the FDA. But the trip from reporting of a finding in a scientific journal to society may be an extremely short one as witness LSD moving from its legitimate research at Harvard rapidly to illicit unsupervised use.

Many times Society is subjected to "experiments" without any regard to ultimate consequences as witness such hazards as air pollution, water pollution, herbicides and many others. Society should have equal rights for the preservation of its health as does the individual. It is time to think through how this laudable aim can be achieved before irre-

But please don't forget this:

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently. Large doses of the alka formulation are contraindicated in glaucoma.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Persistent or severe dyspepsia may indicate peptic ulcer; perform upper gastrointestinal x-ray diagnostic tests if drug is continued. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with caution in the first trimester of pregnancy and in patients with thyroid disease.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. Patients should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make complete blood counts at weekly intervals during early therapy and at 2-week intervals thereafter. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The more common are nausea and edema. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Drug rash occasionally occurs. If it does, promptly discontinue the drug. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Agranulocytosis can occur suddenly in spite of regular, repeated normal white counts. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, hypersensitivity angiitis, pericarditis and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

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Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity* reactions—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

Upon adverse reaction, stop medication and treat appropriately.

Lederle

350-8

parable damage has occurred to Society from scientific discovery which seems quite "innocent" in the laboratory.[4] This study of sex-control can become a prototype for considering how society should protect itself from undesirable effects of scientific discovery.

L.H.N.

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What Makes Gallstones

A recent editorial in the *New England Journal of Medicine*[1] pointed out that despite the frequency of gallstones in the United States research concerning their cause has lagged far behind that in many less prevalent disorders. There is a population of patients, the Indians of the Southwest, who actually has a very high incidence of gallstones[2] and among whom it should be easy to study the composition and physical state of both hepatic and gallbladder bile, for then we could learn what is the initial stage of cholesterol gallstone formation. Is it due to production of an abnormal hepatic bile, to a change of normal bile by the gallbladder or to both?

From Dam et al's studies in the hamster we learn[3] that they have very dilute gallbladder bile and a marked propensity to stone formation. The gallstones can be precipitated by a fat free high glucose diet. These animals develop signs of deficiency of essential fatty acids and liver damage. If, however, they are given a diet high in polyunsaturated fatty acids, previously formed stones will disappear in vivo. Thus it appears that the century old idea that dilute bile has relatively less cholesterol holding capacity than concentrated bile is incorrect. In the hamsters, then it is the liver that is the culprit by forming a dilute bile which can't hold the cholesterol in solution once it enters the gallbladder.

A second possibility is that the liver forms a "normal" bile that is changed by the gallbladder. This was suggested to occur forty years ago when it was shown that bile-salts or acids are rapidly reabsorbed when a gallbladder becomes inflamed. Tepperman[4] showed that mice fed cholesterol and cholic acid develop cholesterol gallstones readily in one month. The cholesterol in this case appears to make the bile more saturated. This may be the mechanism of gallstone formation in patients suffering from hypercholesterolemia.

Burnett[5] made studies on patients during operation for gallstones. He sampled bile simultaneously from the common duct and gallbladder. From his data it appears that gallbladder bile has relatively less bile salts than the corresponding hepatic bile. This suggests that in these patients with chronic cholelithiasis, absorption of bile salts by the gallbladder occurs and it is this factor that may be operating to perpetuate the stones even though the hepatic bile is normal. This effect then incriminates the gallbladder itself where either inflammation, chronic irritation or perhaps irritation by the stones themselves may be responsible.

There are still other processes involved in precipitation of insoluble substances in bile. This is a change that occurs in the normal composition of bile due to the presence of foreign or trace molecules that in turn precipitate the bile and form stones. Calcium bilirubinate stones, calcium glycocallodeoxycholate stones and calcium glycolithocholate stones form due to this cause of precipitation. The first Small[6] points out results from the growth of Escherichia coli. Here free bilirubin combines with calcium to form insoluble stone. The second forms in the presence of high cholesterol in blood and food intake. The third might occur if lithocholic acid is first formed in the intestine due to bacterial overgrowth, absorbed and then secreted into the bile by the liver.

The old ideas that obstruction and inflammation which have been thought of as etiologic mechanisms in cholelithiasis thus are inadequate to explain the overall process of gallstone formation. We have to consider also a change in the relative composition of the bile, such as over dilute bile and bile saturated with high cholesterol. Finally are the infrequent stones precipitated in the gallbladder from asborption of trace elements produced in the intestinal tract.

Now that the ideas of gallstone production have been clarified, it is still impossible to say that in man the initial stage of cholesterol gallstone formation is due to production of an abnormal hepatic bile as in hamsters, to a change of normal bile in the gallbladder as in mice or to a combination of both. To settle this problem it will be necessary to study the composition and physical state of both hepatic and gallbladder bile in patients who are about to form stones.

L.H.N.

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Licorice Hypertension: An Exercise In The Scientific Method

Licorice extract has for many years been used as a flavoring agent in foods, beverages and certain medications. If excessive amounts are ingested then a well defined clinical syndrome appears with hypertension, and at times symptoms of potassium depletion, closely resembling that found in patients with primary aldosteronism.[1] So much so that when Revers[2] employed it in 1946 in a series of patients with peptic ulcer, 20 per cent developed gross edema or cardiac asthma. The aqueous extract of the root of the plant glycyrrhiza glabra has since been purified by Louis and Conn.[1] When they administer it orally in 2-5 gram doses per day to normal subjects, it caused great sodium retention and mild potassium diuresis much as does aldosterone.

Conn et al[1] have recently reported a patient who ingested considerable quantities of licorice flavored candy repeated daily over a period of years. The patient's blood pressure rose gradually. Finally he was given chlorothiazide without response. Thalidone made things worse. He developed muscular weakness and finally paralysis. When at this time serum potassium was determined it was found to be 1.6 mEq. He was treated vigorously with potassium by mouth and intravenously and gradually recovered. It was at this time that aldosterone excretion was determined and found to be one-quarter of normal. After the patient had completely recovered, the whole picture was rapidly reproduced when ammonium glycyrrhizate was administered in graded doses. Months later without licorice ingestion he remained normal.

Conn presents a brief summary of the literature on licorice ingestion and the resulting hypokalemia. Some were caused by administering to tuberculous patients large doses of amino salycilic acid flavored by licorice containing alcoholic beverage called Un Boisson de Coco is marketed and three different groups reported finding persons who consumed one to three liters of this drink per day and developed muscular weakness, at times paralysis with hypokalemia. One patient with reduced aldosterone excretion recovered with spirolactone (aldactone). One case who took large amounts of licorice for weight reduction, developed severe weakness, hypokalemia, and also myoglobinuria.

In patients with primary aldosteronism it is possible for hypertension to occur in the absence of hypokalemia. In Conn's case they considered several possible explanations for his symptoms. One was primary aldosteronism. But he did not have increased secretion of aldosterone. If it were due to licorice, aldosterone secretion should be suppressed as it was. Furthermore, if it were due to the licorice, it should be cured by withholding licorice and administering K. This turned out to be the case. Once recovery had occurred, then the syndrome should recur after resumption of licorice intake, and it did.

The case clearly demonstrated that repeated ingestion of licorice candy did in fact induce arterial hypertension, suppress both aldosterone, and renin activity in a normal individual. Clearly in the presence of hypertension, ingestion of licorice must enter into the differential diagnosis especially if hypokalemia and the resulting symptoms of muscle weakness and positive electrocardiogram is also present.

Overproduction of aldosterone was found to occur in 8 per cent of a large group of hypertensive patients. In each one there occurred suppression of plasma renin activity. One can have hypertension of course even without overproduction of aldosterone and in fact with its suppression as occurs in excessive endogenous production of DOCA. In fact it is possible to develop insidious salt retention with ultimate hypertension developing from unsuspected endogenous factors other than aldosterone and DOCA. The clue to such a mechanism would be the demonstration of the relative sup-

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pression of the entire renin-angiotensin aldosterone system in a hypertensive patient.

Hypertensive patients who do exhibit suppressed plasma renin activity together with underproduction of aldosterone constitute a category in which researchers should hunt for endogenous but also exogenous factors which may promote on a daily basis only minute amounts of sodium retention, but which could eventually lead to hypertension.[3] Neither visible edema nor progressive hypokalemia is a necessary accompaniment of such a slowly progressive process.

Licorice induced hypertension emerges only as a model, but the mechanism through which glycyrrhizic acid induces hypertension may prove to be an important one. It is the same mechanism through which hypertension is produced by aldosteronism. Neither visible edema nor hypokalemia is a necessary accompaniment of such a slowly progressive process.

L.H.N.

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Ecology And Pesticides

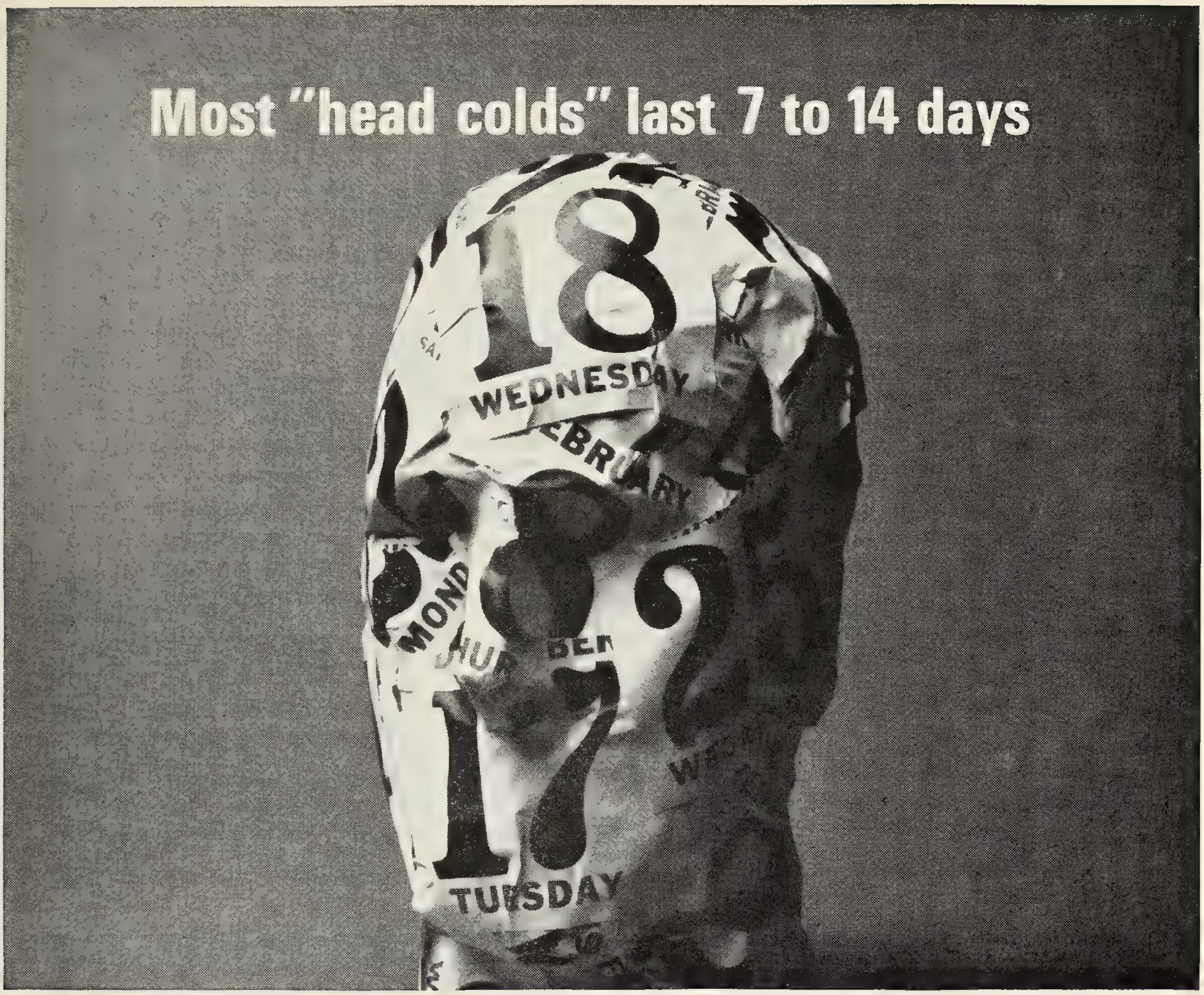
Rachel Carson[1] pointed out in "Silent Spring" that we had lost our perspectives on just how ruthlessly man can treat his environment and still survive. Man was killing pesty insects by the trillions but he was also poisoning natural ecosystems all around him. It is not surprising that she was criticized by special vested industrial interests but praised by the nation's biologists knowledgable in the vital importance of keeping our natural environment healthy. The message of the ecologists is that man in the process of seeking a "better way of life" is destroying the natural environment that is essential to any kind of human life at all. Man has actually made great strides in the direction of ruining the arable land upon which his food supply depends, fouling the air he must breathe and the water he must drink and upsetting the chemical and climatic balances upon which his very existence depends.

The use of pesticides is one facet of man's unthinking assault upon his world. For those who found "Silent Spring" too dramatic an approach to the problem, the gap was filled two years later by "Pesticides and the Living Landscape"[2] in which Ruud further documented Miss Carson's thesis. Now Niering[3] presents us with a review of the literature and his own researches fully confirming that pesticides produce specific physiological effects in animals and man and also effects on the total environment, plants, animals, soil, climate and man. He points out that the real issue is how to employ sound ecological use of pesticides where necessary without drastically contaminating and upsetting the dynamic equilibrium of our natural ecosystem. He goes further to indicate that a small percentage of the money spent on pesticides if devoted to basic research might lead to control of pests without employing poisons that remain permanently in our environment.

Ecologists have long been aware that simplifying the environment to only a few species can precipitate catastrophe. Highly mechanized agricultural operations dominated by extensive acreage of one crop encourages large members of insect pests. Against these pests vast quantities of insecticides are applied with little regard for what happens to the chemical once it is on the land. There is even less regard for the emergence of insect resistance to the sprayed poisons. Before World War II most insecticides were non-persistent organics found in the natural environment such as pyrethrum derived from dried chrysanthemum flowers, nicotine sulphate from tobacco and rotenone from the tropical derris plants.

Now we have potent persistent chlorinated hydrocarbons (DDT and others) to fight the ever increasing horde of insects, now some 3,000 species plaguing man in North America. In 1964 alone industries in this country produced 783 million pounds of pesticides, half against insects and half against vegetation fungi and rodents. The second half has sharply increased since the extensive spraying against vegetations in Vietnam. The application of these chemicals on the natural landscape has now reached the point where one out of every ten acres is being sprayed with an average of four pounds per acre. Dr. George Woodwell[4] estimates that there are now one billion pounds of DDT alone concentrated in the biosphere.

To be sure there are probably positive effects in the form of increased market yields and quality, of agricultural spraying and data from the National Agricultural Chemical Association show that a net increased yield of $5-100 net gain per acre on such crops as barley, tomatoes, sugar beets, pea seed and cotton seed. Such figures are still in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SK&F **Smith Kline & French Laboratories** doubt at least for rice fields. Ruud studied rice crops affected by rice leaf miner outbreak and found only some fields affected, not all. It appears that repeated spraying applications are in many cases actually unnecessary, being used merely as "insurance sprays." The farmer, however, is being forced to this procedure in part by public demand for completely insect-free produce and this has now reached ridiculous proportions. Influenced by advertising the housewife now demands perfect specimens with no thought of or regard for how much environmental contamination has resulted to attain such perfection.

If we could relax standards to a moderate degree pesticide contamination could be greatly reduced. It may be difficult to question that spraying increases the yield and quality of marketable products. But there are few valid data available on how much spraying is necessary, how much it is adding to consumer costs, what further pests are aggravated by spraying and what degree of resistance eventually develops. Insects have a remarkable ability to develop resistance to chemical sprays. Against gnats at Clear Lake, California the third spray was the least effective and now there are over 100 important insect pests that show a definite resistance to chemicals. With so many unknowns should we not seek safer chemical methods and specifically new biological methods to control insect pests. An excellent example are the studies of setting loose natural predators upon the desired insect pest. Another is the attempt to modify the DNA of male mosquitos that could lead to extinction of the species.

The obvious answer to man's destruction of his environment by biocides, is withholding unnecessary spraying and more basic research in pest elimination.

L.H.N.

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To Control Microbiological Warfare

In the past decade much research has been done on microbiological weapons. Presently our government is working on adequate means of delivery of these agents without contaminating our own soldiers.[1] Once this problem is solved, the risk is greatly increased of this type of weapon being employed in war. For this reason there is now the choice between going ahead and securing international agreement for control or doing nothing at all. In the latter case the risks and the fears of eventual use of microbiological methods of warfare will continue and intensify.

The British Government has now proposed the early conclusion of a new Convention for the Prohibition of Microbiological Methods of Warfare which would supplement the 1925 eneva Protocol.[2] This Convention would proscribe for hostile purposes microbiological agents causing death or disease in man, animals or crops. Under it States would: (1). declare their belief that use of microbiological methods of warfare of any kind and in any circumstances should be treated as contrary to international law and a crime against humanity; (2). undertake never to engage in such methods of warfare themselves in any circumstances.

But the whole field bristles with many difficulties. Organisms for biological warfare can be produced quickly, cheaply and easily. Many are required in ordinary and perfectly legitimate ways for production of vaccines. Clandestine research could easily be conducted. Storage is scarcely necessary for chemial plants and breweries could be quickly switched for producing harmful microorganisms in enormous quantities. Only delivery systems are still in doubt.

The Pugwash Conference has indicated possible ways of making inspection effective[3] but judging from its lukewarm reception the proposed Convention seems not to be enough. One important obstacle to any progress on disarmament is the profound suspicion among many countries on each others intentions. Clearly in the absence of trust, treaties cannot be dependable. In its presence they are hardly necessary. Only actions restoring a degree of trust are likely to be effective. Secrecy about microbiological work denitely precludes mutual trust.

A big government like ours could give a sound basis to the Geneva proposal by declaring all future work carried out in this field be declassified at any rate for a trial period. This would carry especial conviction if it were linked to participation with WHO in the large scale production of microorganisms as additions for regions where dietary protein is inadequate. There is another proposal that deserves thought. That is to set up an independent International Microbiological Agency akin to the

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International Atomic Energy Agency. Such an agency could then be a control function in biological warfare to the peaceful applications of microbiology.

Despite all the present secrecy, it seems to be difficult for any country to steal a march on another in this sphere where the essential basic knowledge is known to all. Furthermore, the profit in manufacture of these weapons is so minor compared to that employed in present warfare, that there should be no reluctance on the part of the Military-Industrial Complex to give up this small source of revenue. If then the United States should offer to place its biological laboratories under WHO provided of course Russia and other countries agreed to do the same, the risks would be a good deal less than might be thought.

The fact is that biological warfare is viewed with horror by a large section of the public and even the Military, and committment to it has not yet developed to a stage where reversal is difficult. Unlike nuclear or even many conventional weapons the production facilities can be switched almost over night with but little adaptation to peaceful purposes. If disarmament can be secured in this area, it is quite possible that it could then be achieved also in others. If the fetters of secrecy were discarded and an international orientation adopted more immediate and constructive thought could surely be directed next to feeding the world's billion people who are now undernourished.

These are large and frankly political questions, but they are of pressing concern to the medical profession. Biological warfare implies a misuse of medical science for which doctors cannot evade responsibility. After all, medical knowledge and medical participation are inherent in most of its projects. The professions silence on this issue is liable to be interpreted as consent. The secrecy demanded is contrary to the principles of medical ethics and in fact is totally repected in every other medical activity.

We physicians on graduation now take the Oath of Geneva. Under it we solemnly swear to preserve the sanctity of human life and beyond this we dedicate our lives in the service of humanity. To contribute in any way to the production and use of infectious diseases as weapons would make a shambles of our undertaking as physicians.

L.H.N.

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The "Pill", The Veins And The Payoff

Oral contraceptives must be counted as one of the important new discoveries of this decade. The value of this discovery ranges from the convenience to the individual to the control of an expanding population. It has led to very important societal consequences such as conflicts between the individual conscience and the church dicta. It has given the individual greater freedom in the planning of his family and greater independence in his ability to control his own actions. If and when the control of expanding populations by this means become a reality the societal consequences will be very profound.

Among the controversial disadvantages of the use of these agents are the supposed long term effects on the peripheral veins such as thrombophlebitis and varicose veins. The initial source of concern was the possibility that the "pill" and venous thrombosis were causally related. Studies that followed large groups of women were not definitive. However, recent data[1] seemed to show an increased risk of thrombophlebitis in women using contraceptive drugs in Britain. One question that arises is whether the British experience is also true for this country. Another question arises whether there are other kinds of evidence besides statistical to throw light on the British findings. To examine the concept of a cause and effect relationship between the use of oral contraceptive drugs and venous thrombosis it requires that we clarify the causes of thrombophlebitis as it develops spontaneously, and then seek to relate the effects of estrogens and progestogens in the doses present in the "pill" to these spontaneous causes.

The two factors that are known to be of major importance in the genesis of the venous thrombus (red), are stasis or reduced velocity of blood flow within the veins and increased coagulability of the blood.[2] Neither of these alone is sufficient to lead to thrombus formation. Furthermore the degree of each when combined which are required in any specific situation to lead to thrombosis is not established. This is the reason why the thrombophlebitis which develops spontaneously is so poorly understood. Furthermore studies of the clotting factors as they are influenced adversely by the contraceptive pills have not been decisive so far.[3]

Regarding stasis, one well controlled study has demonstrated that the oral contraceptive drugs can cause the veins to dilate abnormally, but the doses required to achieve this are far in excess of the therapeutic doses found in the "pill". It is true that similar dilating effects can be observed in pregnancy, but here again we are dealing with a situation entirely different from that found when a non-pregnant woman is on the "pill". During pregnancy there is both pressure on the veins retarding blood flow in the legs and large doses of estrogens. We know from experiments with large doses of estrogens that veins do dilate and also know that dilated veins occur in rabbits during pregnancy and following administration of large doses of contraceptive agents. Here again, however, the experimental observations are not applicable to the situation found in a non-pregnant woman.

The hormones present in the body during pregnancy while similar to those found in the oral contraceptive agent are of a much higher concentration and this renders a comparison of the state of the veins between the pregnant woman and the non-pregnant woman taking the contraceptive agent quite inapplicable. Even if the changes in distensibility of the veins can be caused by excessive doses of estrogen, we still do not know how much stasis in leg veins result from the use of the contraceptive agent in the non-pregnant female or in fact if any results at all.

It is a physiological fact that if venous dilatation of a sufficient magnitude occurs and the volume of blood flowing through the lower extremity in a unit of time, that is blood velocity, does not keep pace with the dilatation then the venodilatation could act to decrease the velocity of blood flow. How much dilatation occurs and how reduced is the velocity in a woman on contraceptive drugs is however not known. For this reason theorizing about venodilation and reduced blood flow as if this is equivalent to stasis can lead to a wrong conclusion.

Another idea raised about the use of contraceptive agents is the fear that they may contribute to the formation of varicose veins. The argument runs somewhat as follows: if chronic dilatation of the veins has the potential for producing varicose veins and if patients who develop varicose veins have naturally a tendency to increase in distensibility of their veins, then any agent which further promotes distensibility may contribute to development of varicose veins. The contraceptive agents in large doses cause veins to dilate. Therefore the contraceptive agents may contribute to development of varicose veins. It can be seen that this syllogism is based on several assumptions and to verify the conclusion will require much more data than is available at present. Under these circumstances we must operate on the principle of payoff.

Payoff is the positive or negative result in gain or loss which accrues from a particular outcome. The clinician is one player and nature in the form of disease the other. The physician is guided in his decision-making process under a given situation as to what will happen to the patient if in this case she takes the pill or if it is withheld. If she takes the pill she will avoid pregnancy, she will have a reduced incidence of cystic mastitis and of cervical cancer.[4] Besides this are the psychological benefits deriving from confidence in avoiding unwanted pregnancy. Against this, of course, the physician must weight the consequences of not prescribing the pill, such as pregnancy and the consequences arising from this event.

As regards the veins, in this country the annual death rate of non-pregnant women from pulmonary embolism among users of the pill is less than 1.5 per 100,000 for those in the age group from 20-34 and 3.9 for those in the age group from 35-44. However, if the pill is withheld the death rate rises markedly during pregnancy when 7.5 per 100,00 occurs for these 20-34 and 13.8 per 100,000 for those from 35-44. The latter do not include deaths from other complications of pregnancy such as abortion, complications of delivery, phlebitis, thrombosis and embolism after pregnancy. Altogether the risks of death from pregnancy, delivery and pureperium is 22.8 for women between 20-34 and 57.6 for those between ages 35-44.

Another significant fact to take into consideration is that although the use of the pill has markedly increased, the reported rates of pulmonary embolism during this period has not increased proportionately.

It is true that some physicians advise against the use of the pill in women who have had thrombophlebitis, the fact however is clear that if we consider the principle of payoff the risk of using the pill is less than that of not using it except for rare exceptions.

L.H.N.

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To Train Not Strain

Life expectancy in the United States is not changing very much despite advances in medical research and medical practice. For an explanation of this paradox we must search for counterbalancing factors in deleterious living patterns. Some are due to life years lost by accidents upon the highways. Some by life years lost in war. This combination of killing the young people is a greater loss to society in life years than is heart disease. This last, however, is the number on killer, is increasing and contributing heavily to it are such controllable factors as sedentary living, obesity and excessive cigarette smoking.

The Framingham study has identified many factors contributing to heart disease. In one of its contributions it examined the role of physical activity. The most sedentary individuals had a mortality from coronary heart disease five times that of individuals who were active. At first thought we might think clustered among the sedentary individuals are also those with unrecognized heart disease. But this cannot be the whole story for several reasons. One is the confirmatory findings by Frank and his colleagues[1] who have studied coronary heart disease occurring in a defined population of 110,000 men and women. They have noted that the incidence of rapidly fatal myocardial infaction among sedentary individuals who are smokers is nine times the incidence among physically active non-smokers of similar age. Another is the well recognized fact that exercise increases the coronary circulation and by this means would tend to prevent or minimize myocardial infarction. Another is that active individuals are less likely to be overweight.

Physicians have long recommended[2] physical fitness including weight control but the admonitions usually are not accompanied by realistic prescriptions. A physiological way to reduce weight is to eat a balanced diet representing a modest caloric deficit with respect to ordinary needs and to attain a further caloric deficit through exercise. This means that weight losses of half to one pound a week can be achieved comfortably. Two recently issued paperback books[3] give simple effective programs of exercise for improving physical fitness. The books emphasize the great importance of conditioning the cardiovascular system. The value of isometrics are questioned and calisthenics are assigned a secondary role.

The cost in time and effort in achieving fitness is small. Apparently not more than one to two hours a week of effort is required although to establish the correct habits one should split it among three or four occasions and preferably daily. In sixteen weeks or less sedentary individuals can note profound changes in their physical condition. For example the resting pulse rate may be lowered from 85 to 65 beats per minute and the time required to go a mile may be cut from 12 to about 8 minutes.

As physicians we must recognize two precautions in advising undertaking of phyiscal conditioning. It is well for the patient to have a proper physical checkup before expanding his activity. The second is to recognize that in the conditioning process one should train not strain. The programs begin with easy tasks for example one mile of walking, and as fitness improves to progress to more exacting efforts. The recommended means for maintaining fitness is jogging or running. However, other activities such as cycling or swimming are also effective. Cooper[4] discusses the relative benefits of the various forms of exercise. As one result of the conditioning process the heart becomes much more efficient. Åstrand[5] has calculated that by expending some 2,000 extra heart beats during the daily exercise, one saves up to 30,000 heart beats over the remainder of thetwenty-four hours.

One important potential benefit from physical fitness is an improvement in mental attitude and emotional relaxation. As Abelson points out in *Science* the typical middle-aged sedentary individual is in effect "crawling submissively to the grave." By investing several hours a week he can add years to his useful life.

While it is desirable for a younger man still in good condition to build up his practice for exercise to a half hour daily, it is also true that three fifteen minute periods of intensive exercise a week together with daily hour of walking are sufficient to improve cardiovascular fitness. This will enable him to become a better athlete than many who are twenty to thirty years younger. Buoyed by pride and a sense of well being he can compete more confidently in intellectual areas.

L.H.N.

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Letter To The Editor

Dear Dr. Richards:

The editorial staff of *Connecticut Medicine* should be complimented for their extensive September issue appropriately timed to coincide with "Family Practice Week," as proclaimed by Governor Dempsey. It was an excellent compilation of articles used to show the present plight of the family practitioner.

In order to insure a continued supply of family practitioners, a concentrated effort has to be made to create a new image for those practitioners who are in the front lines of medical delivery. This effort has to be made by medical educators, the hospitals, as well as the threatened medical practitioners, to eliminate the snipers; otherwise it will be the old story of "too little too late" for this time-honored system of personal medical care.

Yours truly,
Yale Gordon, M.D.
Elmwood, Conn.

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

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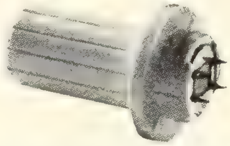

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The Hartford Hospital Inter-Departmental Conference

Thromboembolic Disease

Phillip Trowbridge, M.D.

Dr. Phillip Trowbridge: The topic for discussion this morning is venous thromboembolic disease. Yearly in this country at least 40,000 persons die from pulmonary embolism. The true incidence of thromboembolism is difficult to ascertain. However, careful autopsy series reveal an incidence as high as 65%. Thromboembolism all too often occurs in young people, and in patients in whom recovery was otherwise expected. Many terms are used in referring to venous thrombotic disease—phlebothrombosis, superficial thrombophlebitis, deep thrombophlebitis, phlegmasia cerulea dolens, and others. Dr. Coley, are these all separate entities, or a spectrum of the same disease?

Dr. Geoffrey Coley: It was formely felt that "phlebothrombosis", or "bland thrombophlebitis", differed from inflammatory, deep, thrombophlebitis, and that "phlebothrombosis" carried a higher risk of pulmonary embolization, presumably because this was intravascular coagulation rather than inflammation of the intima. At present, such a distinction is considered invalid. The spectrum of phlebitis ranges from slight inflammation to the massive venous occlusion that results in phlegmasia cerulea dolens. One is probably as dangerous as the other.

Dr. A. C. DeGraff, Jr.: The difference between deep and superficial thrombophlebitis may simply be due to the size of the vessel involved. Emboli from small superficial vessels may be so readily cleared by the lungs that they are not clinically apparent.

Dr. Charles Bucknam: The point should be made that although phlebitis is associated with varying degrees of inflammation, there is no bacterial infection, and usually no need for antibiotics.

Dr. Trowbridge: What produces phlebitis? Is there a particular group of patients who have a high risk of phlebitis?

Dr. Buchnam: The cause of phlebitis is not known, but there are 3 accepted predisposing factors: 1.) stasis, 2.) trauma to the vessel and 3.) a hypercoagulable state. Stasis may occur in patients with congestive heart failure or in patients on prolonged bed rest. Trauma may be direct, as in fractures or injury, or secondary to surgical manipulation of the veins in the involved area. A hypercoagulable state is difficult to prove.

High risk patients include the obese, those with previous thromboembolic disease, those with malignant tumors, and those undergoing pelvic surgery in the vicinity of the large vessels. The incidence of thromboemboli in a high risk control group is reported about 10% in contrast to 1% in a high risk group treated with warfarin. Heparin is also effective and may actually be preferable.

Dr. David Hochberg: Several reported studies indicate that thrombophlebitis and pulmonary embolus often follow major surgery. The rationale for prophylactic anticoagulation is to lower this incidence. For example, after cholecystectomy, 3 to 4 percent of patients develop thrombophlebitis and 0.5% have pulmonary emboli. After pancreatic surgery the incidence of thrombophlebitis may be as high as 13%. While fatalities after hernia surgery are rare, 75% are caused by pulmonary emboli. Statistically, the incidence of pulmonary emboli rises sharply on the 4th or 5th postoperative day and they occur predominately in patients over 50 years of age.

Dr. Trowbridge: A pulmonary embolus may be the first clinical sign that the patient has thrombophlebitis. However, it has been stated that in as many as 75%, premonitory signs of venous obstruction could have been detected by careful examination. How should we approach this problem?

Dr. Coley: I would think 75% is too high, and would say perhaps 30 to 50%. Differential calf

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Moderator:

PHILLIP TROWBRIDGE, M.D., Department of Surgery.

Discussants:

GEOFFREY COLEY, M.D., Department of Surgery.

ARTHUR C. DEGRAFF, JR., M.D., Pulmonary Section—Department of Medicine.

CHARLES BUCKNAM, M.D., Cardio-vascular surgeon—Department of Surgery.

DAVID HOCHBERG, M.D., Resident Physician—Department of Surgery.

JACK WESTCOTT, M.D., Department of Radiology.

WILLIAM C. HARVEY, M.D., Resident Physician—Department of medicine. Hartford Hospital. Hartford Conn. 7/1/65-6/30/68.

measurements, Homan's sign, etc., may be helpful but usually are determined only after symptoms are present. I don't think we can rely on physical findings to solve the problem of thromboembolism.

Dr. Trowbridge: Dr. Westcott, what radiologic aids help detect venous thrombosis?

Dr. Jack Westcott: For the deep veins, their location, number and patency can be determined by venography, which is a fairly simple procedure. However, the normal variations in size, location, and number of the perforating superficial veins makes it almost impossible to determine the presence or absence of thrombosis in them.

Dr. Bucknam: One reason these thrombi are difficult to detect before they embolize is that most are only partial thromboses, not completely occluding the vein. An embolus is often the first indication of thromboembolic disease, unless there happens to be related tenderness or pain. There is no local hemodynamic problem until the vein is totally occluded. However, I strongly advocate early venography after a suspected pulmonary embolus.

Dr. Trowbridge: Dr. DeGraff, what happens when an embolus reaches the lung?

Dr. DeGraff: We probably all have pulmonary emboli at some time in our lives. Following even minor surgery platelets aggregate. Some break off and pass to the lungs where they lodge in the pulmonary vessels. The vast majority of these are not serious because they are small and are rapidly cleared by macrophages. The lung functions as the major clearing organ in the body, the only organ through which 98% of the blood passes during a single circulation. In a peripheral clot, a highly polar polypeptide, which is felt to be strongly vasoactive*, is released into the venous circulation and then as it passes through the lungs comes into contact with and presumably binds to the walls of small pulmonary arteries. The concept of binding of a vasoactive polypeptide which produces pulmonary vasospasm may explain why a a patient with an apparently insignificant embolism may die with pulmonary vascular obstruction.

The purpose of therapy is to stop the formation of clots. As long as there is an actively-forming clot, the potential for continuing pulmonary vascular spasm exists. The only substance which has been clearly shown to stop the formation of clots is heparin.

Dr. William Harvey: I agree, heparin is superior to the warfarin group of drugs, in preventing both intravascular coagulation and thrombosis. One great advantage of heparin is that the patient can be ambulated almost immediately, and this obviates the danger of prolonged bedrest and venous stasis. The Scandinavians who have well-documented their experience with heparin give large doses: 100,000 units the first day, 40,000 units the second day, then taper and conclude in 7 to 10 days. Stamm**, in Switzerland reviewed the world literature on thromboembolic fatalities in patients treated with heparin. In the 500 cases reviewed, no fatality was recorded in any patient receiving more than 40,000 units per day. At doses of 40,000 units there is a substantial incidence of clinical bleeding, but any less increases the incidence of fatality from thromboembolism. The clotting time must be far beyond its normal range. Experimentally it must be elevated in excess of 30 minutes for therapy to be effective. After two or three days of empirical therapy the clotting time should be obtained about an hour before a dose of heparin and should be in excess of 20 minutes. Thereafter the clotting time need be performed only once or twice a week. Ten thousand units of heparin, intravenously, every 6 hours is probably effective. If the bleeding is minor, simply reduce the dose; if more severe, stop the drug; and if the bleeding is life-threatening, give the heparin antidote, protamine. There are no firm criteria for how long to continue therapy. but Bauer*** suggests 10 days and Stamm 21 days.

Dr. Trowbridge: Dr. DeGraff, let us consider a hypothetical patient who has been in bed several days, has coronary artery disease, suddenly complains of chest pain, becomes hypotensive, sweaty, dyspneic and cyanotic. How do we differentiate pulmonary embolus from myocardial infarction or dissecting aneurysm?

Dr. DeGraff: Even a careful history and physical examination and an electrocardiogram may not establish the diagnosis. The serum LDH and bilirubin may help, but not in the immediate situation.

The only diagnostic criterion is a pulmonary angiogram. However, if the angiogram is postponed a day or two, it may be too late because the pulmonary macrophages are so efficient they may clear even large emboli.

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* McClement, John. From an address to the Respiratory Group of the Physiology Society, 1967.

** Stamm, H. Current use of heparin in venous thrombosis *Thromb. et Diath. Hemorrh.* 9 (Suppl. 11): 61, 1963.

*** Bauer, G. Clinical experiences of a surgeon in the use of heparin *Amer. J. Cardiol.* 14:29, 1964.

I have not found the lung scan to be very helpful. Patients often have a radiographic pulmonary infiltrate which gives a false positive result and an abnormal lung scan. If, however, the lung fields are clear by chest x-ray and there is no clinical pulmonary disease, then an abnormal lung scan would be helpful.

Dr. Trowbridge: Dr. Westcott, how technically difficult is the pulmonary angiogram?

Dr. Westcott: It is not difficult. It is simply a matter of getting enough contrast medium into the heart or the pulmonary artery to show the pulmonary vascular bed. In heart failure, the contrast medium is diluted and the quality of the angiogram may be poor. We have no mortality from angiography but have observed transient arrthythmias, hypotension and tachycadia. Occasionally contrast medium has been deposited in the wall of the heart. This, however, has been of no apparent clinical significance. Patients with large pulmonary emboli seem to tolerate pulmonary angiography. Most deaths have occurred in patients with chronic pulmonary disease, particularly cor pulmonale. The patient with heart failure, the most technically difficult, often has the least reaction, probably because the contrast medium is so diluted.

If the quality of the angiogram is good, we can probably detect most sizeable emboli, but not multiple small, peripheral emboli. Other pathologic conditions cause a similar angiographic appearance. For example, emphysema and fibrosis will cause a similar lack of perfusion and is difficult to differentiate.

Concerning the lung scan, any disease will alter it—even bronchial asthma. Although the lung scan may not help in diagnosis of a pulmonary infiltrate, if the routine chest x-ray is clear, the scan can be extremely valuable in diagnosis and, even if there is one pulmonary infiltrate, the lung scan may show a defect in another area that is clear on routine chest x-ray.

Dr. Trowbridge: Not all patients who have pulmonary emboli respond satisfactorily to anticoagulants. Dr. Bucknam, would you address the subject of pulmonary embolectomy and vena caval ligation?

Dr. Bucknam: In such a patient, having conclusively demonstrated a pulmonary embolus, two steps must be considered: (1) vena caval ligation, or clipping; (2) pulmonary embolectomy. In the patient with a generally good prognosis, clipping of the vena cava and a thrombectomy are indicated if a major ileofemoral thrombosis is demonstrated. Pulmonary embolectomy should be reserved for those patients in extremis and those in shock, who do not respond to vasopressors. If the blood pressure cannot be maintained and the pulmonary angiogram shows a definite pulmonary embolism, this patient should be considered for partial bypass followed by pulmonary embolectomy. Of the 130 cases recently reviewed, 40% have survived.

Dr. Trowbridge: When you do a pulmonary embolectomy, do you ligate or clip the vena cava at the same time?

Dr. Bucknam: Following a pulmonary embolectomy, the vena cava should almost always be clipped. One further comment about ileofemoral disease: Heparin therapy alone is not necessarily adequate in every case of thrombophlebitis. Evidence is accumulating that some patients do better if the clot is surgically removed. Certainly, this is controversial, but reports are becoming more frequent and more enthusiastic. It is felt that after clot removal, the function of the venous valve is retained, which is not the case with heparin therapy alone.

Dr. Trowbridge: In summary, the problem of thromboembolic disease is significant both in medical and surgical illness, so significant that certain groups of patients seem to profit from prophylactic anticoagulation. The manifestations are often subtle and the diagnosis frequently difficult. The lung scan and pulmonary angiography are frequently helpful despite their known limitations. Constant physician alertness is probably the best defense. Heparin is currently the drug of choice for treatment. The role of peripheral thrombectomy is still under evaluation. Pulmonary embolectomy should be reserved for those patients who are refractory to all other measures.

X-ray: G.I. Seminar

Fever, Diarrhea and Abdominal Pain

Murray A. Rosenberg, M.D. and William A. Hoffman, M.D.

Dr. Rosenberg: Gentlemen, I present the films of an eighteen year old white female admitted to the hospital with a three week history of recurrent crampy pain in the right lower quadrant of the abdomen. She also had chills and fever. There was a history of weight loss and recent anorexia. She passed frequent watery stools varying in color from yellow to green but there was no bleeding. A grapefruit size, nontender mass was palpable in the right lower quadrant. Pelvic examination revealed a firm, slightly tender mass high in the right side of the pelvis. The hemoglobin was 12 grams per cent. The white blood count was 16,000 with 69 polys, 12 stabs, 13 lymphs, 4 eosinophils and 2 monocytes. The urinalysis, blood serology and pregnancy test were negative. Stools for ova and parasites and pathogenic bacteria were negative. The family history and past history were unremarkable. Dr. Marshak would you like to discuss the X-ray findings and offer a roentgen diagnosis? Figure 1 is a representative film of the barium enema and Figures 2 and 3 are early and late films of the small bowel series performed the day following barium enema.

The patient was placed on an antibiotic and bedrest. She showed a remarkable clinical response. The mass subsided and the fever, chills, and diarrhea abated. The patient was able to return to work within two weeks following dismissal from the hospital.

Dr. Marshak: Barium enema examination reveals a free flow of barium from rectum to cecum. The cecum and ascending colon are markedly spastic

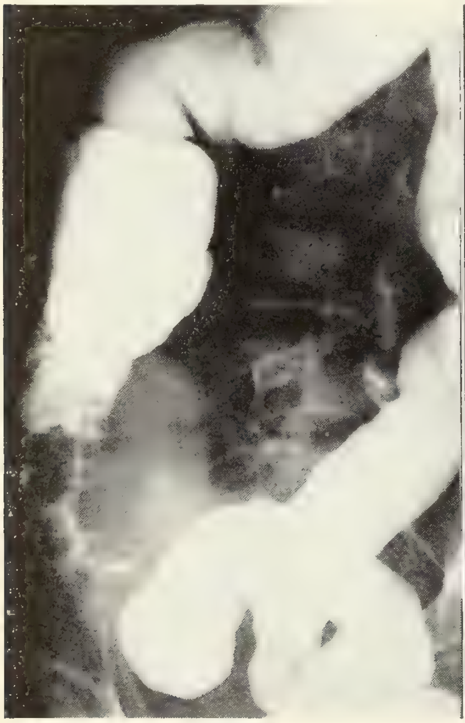

Figure 1

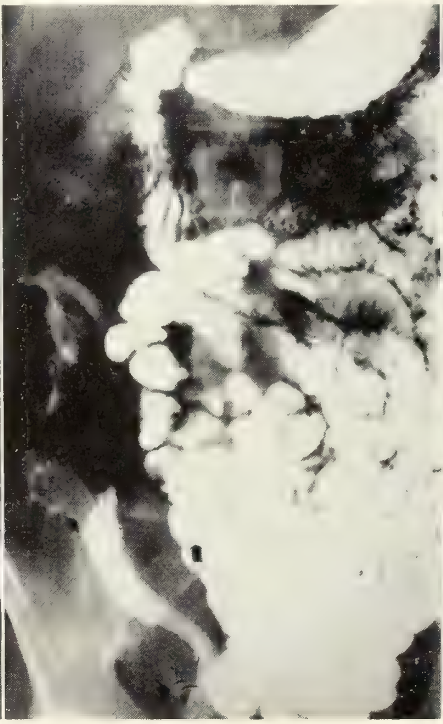

Figure 2

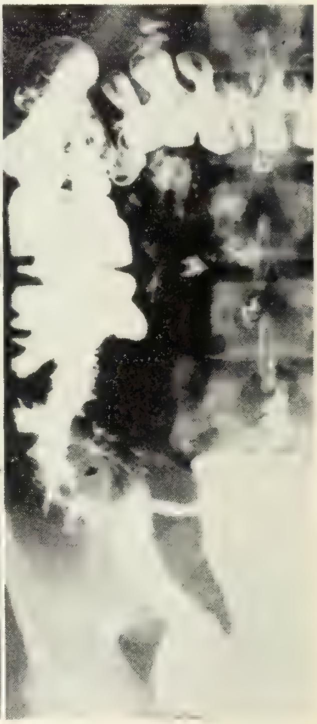

Figure 3

Panelists for this session of our simulated Grand Rounds:

Richard H. Marshak, M.D.: Clinical Professor of Radiology Mt. Sinai School of Medicine, Attending Radiologist, Mt. Sinai Hospital, New York.

Samuel D. Kushlan, M.D.: Clinical Professor of Medicine Yale University School of Medicine, Associate Physician-in-Chief, Yale-New Haven Hospital.

DR. MURRAY A. ROSENBERG, Attending in Radiology, Park City Hospital, Bridgeport, Assistant Clinical Professor of Radiology, Albert Einstein College of Medicine, New York.

DR. WILLIAM A. HOFFMAN, Attending in Medicine, Park City Hospital, Bridgeport, Clinical Assistant Professor of Medicine, Yale University School of Medicine, New Haven.

and irritable with distorted and thickened folds. No discrete ulcerations are identified and there is no reflux into the terminal ileum. The remainder of the colon is normal.

The small bowel series reveals the distal 9 inches of ileum to be involved with a granulomatous inflammatory process characterized by a moderate degree of narrowing, rigidity, ulceration of the mucosa, slight irregularity of the contour and separation of the loops of bowel secondary to the thickened wall and the indurated mesentery. (Arrows)

The findings in the cecum and ascending colon are again identified. The folds are thickened, spastic and irritable. The appendix is visualized in the right lower quadrant and a small sinus tract may be present extending from the cecum into the distal portion of ileum. (Arrow) No other sinus tracts or fistulae are identified. The remainder of the small bowel is normal. No significant obstruction to the flow of barium is noted.

IMPRESSION: The findings are classical for granulomatous ileocolitis. Although it was quickly realized that this entity can involve the entire small bowel and the stomach the concept that it involved the colon was not accepted as readily. Colp reported the first case in 1934 and more recently there have been a flow of reports on involvement of the colon.

Dr. Rosenberg: The spleen was questionably palpable but was felt to be enlarged by x-ray. Does this alter your impression?

Dr. Marshak: It is not unusual for the spleen to be slightly enlarged in regional enteritis. As a matter of fact in review of our cases, splenic enlargement was more common in regional enteritis than in lymphosarcoma involving the small bowel.

Dr. Rosenberg: Would you consider ilececal tuberculosis or intestinal amebiasis in your differential diagnosis? I might add that her chest x-ray and intravenous urogram were negative.

Dr. Marshak: In differential diagnosis the following should be included;

1. *ILEOCECAL TUBERCULOSIS:* Ileocecal tuberculosis may be indistinguishable from regional enteritis. Fortunately this entity is uncommon and therefore should only be considered lightly in the differential diagnosis. Tuberculosis of the intestine occurs with a negative chest x-ray and the diagnosis usually comes as a surprise. Helpful in the diagnosis is the tuberculin test. This is frequently negative in regional enteritis and of course positive in tuberculosis. On occasion tuberculosis causes marked irregularity of the ileocecal valve and more irregularity of the small bowel.

2. *LYMPHOSARCOMA:* Lymphosarcoma can involve the terminal ileum and the cecum and may produce alterations that are difficult to differentiate from regional enteritis. In lymphosarcoma, however, there are usually tumor nodules of varying size. The lumen is not significantly narrowed because lymphosarcoma is a medullary tumor with little desmoplastic reaction. Thickening of the wall occurs because of submucosal infiltration, but the thickening of the wall and the enlarged mesentery is also noted in regional enteritis. In the latter disease ulceration of the mucosa is severe in most instances, producing either diffuse ulceration or cobblestoning and a symmetrical pattern not seen with a tumor. Sinus tracts and fistulae are larger and longer in lymphosarcoma.

3. *AMEBIASIS:* Amebiasis is uncommon in our vicinity and is usually limited to the colon. It is possible for amebiasis to produce granulomatous changes and a typical appearance of granulomatous colitis. The characteristic findings in the terminal ileum in this case is against the diagnosis.

4. *INFARCTION OF THE SMALL BOWEL:* Infarction of the small bowel may mimic the roentgen findings in regional enteritis. Initially, however, there is spasm and irritability which proceeds rapidly to edema of the folds and stenosis. These cases practically always involve the small bowel in young people and the colon in old people. Intramural bleeding into the wall such as seen with anticoagulants produce thickened folds which are pliable and neat with no evidence of ulceration. The alterations disappear when the medication is discontinued.

In summary we are dealing with a patient with granulomatous ileocolitis.

Dr. Hoffman: Dr. Kushlan are you satisfied with the radiologic diagnosis in patients with regional enteritis?

Dr. Kushlan: From my own standpoint as a gastroenterologist, the radiologic diagnosis in patients with regional enteritis is usually quite definite and satisfactory. Although there may at times be some question as to the diagnosis from a purely radiologic standpoint, when combined with the usual clinical features of chronic febrile nonbloody diarrhea in a young adult, any doubt is usually dissipated and the diagnosis then "clinched". In addition, as pointed out by Dr. Marshak, the radiologic features of regional enteritis are rather distinct, usually leading to a definitive diagnosis without the support of the clinical data.

Dr. Hoffman: When do you favor surgery to establish the diagnosis and rule out other diseases such as lymphoma?

Dr. Kushlan: Except for the occasional cryptic situation in my experience surgery has rarely been necessary to establish the diagnosis of regional enteritis. Again, chronic febrile non-bloody diarrhea in the young adult, with confirmative x-ray evidence of regional enteritis, usually makes further investigation unnecessary, in the context of the question. Surgery to establish the diagnosis becomes a practical necessity if the patient fails to respond to the usual medical therapeutic measures, or does not present a diagnostic radiologic picture.

Dr. Hoffman: What are your opinions regarding steroid treatment in regional enteritis?

Dr. Kushlan: In my opinion, cortico steroids represent the treatment of choice in regional enteritis where they are used essentially as in ulcerative colitis. In my experience, the results of such treatment in regional enteritis are almost, but not quite, as good as they are in ulcerative colitis. Antibiotics are usually not very effective, though they appear to have been so in the patient presented. My experience with Azulfidine has been as disappointing in regional enteritis as it has been in ulcerative colitis.

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We are spinning our own fates, good and evil and never to be undone. The drunken Rip Van Winkle in Jefferson's play excuses himself from every fresh dereliction by saying "I won't count this time." Well he may not count it, and a kind Heaven may not count it, but it is being counted none the less. Down among his nerve cells and fibers, the molecules are counting it, registering it, and storing it up to be used against him the next time temptation comes. Nothing we ever do is, in strict scientific literalness, wiped out. William James. *Essay on Habit.*

Hepatic Dysfunction of Pregnancy

William C. Harvey, M.D.

Introduction

In 1954 the Swedish investigator Svanborg[1] discussed a situation originally described by Ahlfeld in 1883,[2] and presented an argument sufficiently compelling to make it acceptable as a disease entity. This condition has been variously called hepatosis, jaundice of pregnancy, recurring idiopathic jaundice of pregnancy, benign jaundice of pregnancy, recurrent intrahepatic cholestasis of pregnancy, or, as the author prefers, hepatic dysfunction of pregnancy. Many physicians have undoubtedly seen examples of this disease, perhaps presenting as "pruritus of pregnancy." In 1955 Thorling reported a series of 36 patients.[3] Since he was also Swedish, it became known as a disease of Scandinavians. However, by the time of a major review by two Swiss, Haemmerli and Wyss, in June 1967,[4] it had also been reported in England, Austria, Switzerland, France, Belgium, Italy, Poland, Rumania, Chile, Argentina, India, Canada and the United States and is thus of widespread occurrence.

By their very strict criteria Haemmerli and Wyss[4] accepted only 43 of the 132 reported cases. However, they estimate that it accounts for 20 to 50% of all cases of jaundice occurring during pregnancy, a very considerable portion, indeed. Kreek, Sleisenger and Jeffries in a prospective study, using somewhat more liberal criteria, found 14 cases of the disease in the first 400 pregnant patients they screened.[5] While the exact incidence is still unclear, it is apparent that this condition merits increased attention as a major complication of pregnancy.

While it has been termed benign jaundice, the accompanying pruritus is so severe as to be highly demoralizing and debilitating to the mother. Moreover, there is considerable doubt whether the process is benign for the fetus. For these reasons, diagnosis is of importance since a highly effective symptomatic treatment is available. In addition, investigation of cases has yielded very interesting and fundamental observations on pregnancy, hormones and the liver.

Description

The clinical disorder, hepatic dysfunction of pregnancy, is entirely distinct from the 47 described cases of acute fatty metamorphosis of pregnancy or the pathologically indistinguishable cases of fatty metamorphosis associated with tetracycline therapy. The early descriptions of this disease indicate that it began in the third trimester of pregnancy as pruritus which is followed by hyperbilirubinemia which may or may not result in jaundice. There are no other symptoms of physical illness. The only signs are the results of scratching, a variable degree of clinical icterus, and a liver which is sometimes one or two fingerbreadths palpable and variably tender, but not actually enlarged. Specifically, there are no stigmata of cirrhosis, nor is the spleen enlarged. The blood alkaline phosphatase is usually moderately elevated (100 to 300 I.U.). The serum transaminases are modestly elevated (e.g. SGOT and SGPT 100 IU/L) and the bilirubin varies from 2 to 8 mg.%. The thymol turbidity and cephalin flocculation are normal as are the serum proteins. Occasionally, the prothrombin time falls slightly to 30 or 40% of normal. The pruritus and jaundice subside almost immediately upon delivery, and subsequent pregnancies are almost invariably attended by the same happenings to a greater or lesser degree.

As a result of the tabulation of numbers of cases, some earlier clinical notions have been revised. While this condition was felt originally to appear as a complication of the third trimester, it has been reported as early as the 7th week, and the mean onset is actually 26 weeks.[4] There has been no prediliction to age or race, although a familial incidence has been observed. Holzbach and Landers[6] in tabulating 85 cases in 1965 found 13 cases occurring in five families, suggesting the possibility of an hereditary mechanism of unknown nature. There has been no association with other complications of pregnancy, for example, diabetes, pyelonephritis, or toxemia.

Several authorities, including Eastman and Hellman,[7] have concluded that the disease is benign to both mother and fetus. While severe, generalized

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The views expressed herein are those of the author and do not necessarily reflect the views of the Air University, the United States Air Force, or the Department of Defense.

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pruritus may not be life-threatening; neither is it "benign" for those patients who have been subjected either to diagnostic laparotomy or to therapeutic abortion.[8]

Fetal Mortality

Concerning the fetus, several observers have commented on a tendency to premature delivery. Thus, in Thorling's series of 36 patients[3] the average gestational age was three weeks less than his control population. Prematurity has also been mentioned in isolated case reports.[5, 9, 10] Haemmerli and Wyss believed that prematurity tends to recur in certain, but not all individuals with the disease. This, of course, would affect the mean gestational age. They conclude that this "condition is entirely benign to both mother and child"[4] which certainly is not true of the selected recurrent cases they describe.

In two series the actual incidence of fetal mortality is reported (see Table I). Ikonen[8] states that in 73 pregnancies in 65 patients there were 18 deaths (mortality rate 25%). There were three deaths due to artificial termination of pregnancy, two were deaths of a twin and not further described, one infant died after delivery in the 30th week, two intrauterine deaths were thought due to toxemia, two died of Rh incompatibilities, three had developmental abnormalities, and the remaining five were unexplained deaths in term infants.

TABLE I

Series	*Deliveries*	*Deaths*	*Mortality*
Ikonen (1964)[8]	73	18	25%
Haemmerli and Wyss (1967)[4]	22	5	23%
Total	95	23	24%

Of the 22 children born to the six patients reported by Haemmerli and Wyss, there were five deaths (mortality rate 23%). One term infant had undetectable prothrombin levels and died, despite vitamin K therapy, of a massive subdural hematoma. (The maternal prothrombin time was 37%.) A premature infant died of pneumonia (28 weeks) and another who weighed 1120 Gm. died of "immaturity." One term infant died from "massive meconium aspiration," and the fifth child died from congenital heart disease thought due to maternal rubella in the first trimester. Thus, the mortality rate among 95 infants in these two series is 24%. The causes of death in both series are listed in Table II. This is a very disquieting figure, and until it is explained, we can no longer assume that hepatic dysfunction of pregnancy is benign for the fetus.

TABLE II

CAUSES OF DEATH IN COMBINED SERIES

Cause	*Number*
Unexplained (term)	6
Prematurity (1 pneumonia)	5
Developmental abnormality (? 1 rubella)	4
Rh incompatibility	2
Toxemia (in utero)	2
"twin"	2
Subdural hematoma (0% prothrombin time)	1
Meconium aspiration	1
Total	23

Pathology

In 28 of the reported cases (Haemmerli and Wyss) liver biopsies have been performed. These showed no cellular infiltration or hepatic necrosis, but there was dilatation and plugging of the smallest biliary radicals. Electron microscopy has shown variable mitrochondrial abnormalities and has consistently shown distortion of the microvilli of the bile capillary. Post-partum liver biopsies have always been normal as have post-partum liver function tests.

Representative chemical abnormalities are shown in Table III. Taken together they indicate a mild and rather nonspecific hepatic disorder They are decidedly unlike viral hepatitis, but they are not incompatible with biliary tract obstruction or cirrhosis and are virtually indistinguishable from drug-induced cholestatic jaundice.

TABLE III

REPRESENTATIVE LIVER FUNCTION TESTS

Bilirubin	2.0 mg.% (range 1.5 to 8.0)
Alkaline phosphatase	120 IU (range 100 to 300)
SGOT	120 IU
SGPT	100 IU
TT	2.0
CF	0/0
TP with A/G	6.2 (4.2/2.0)
BSP	12% (range 10 to 25%)

Etiology

In this disease pruritus ends almost immediately the patient is delivered. The bilirubin falls rapidly followed by the alkaline phosphatase, and in ten days the patient is asymptomatic; the liver tests and biopsy are normal. It was appreciated very early that the key event might be the loss of the placenta, leading various authors to speculate that the cause of this disease might reside in the placenta.[11-13] The most likely possibility seemed to be the hormones of pregnancy. (The placental hormone production increases throughout pregnancy as shown in Figure 1.) In 1965 Sallomi and Belew reported a patient who did not experience the expected cure at delivery.[14] After three weeks, retained secundines were evacuated, and the patient promptly improved.

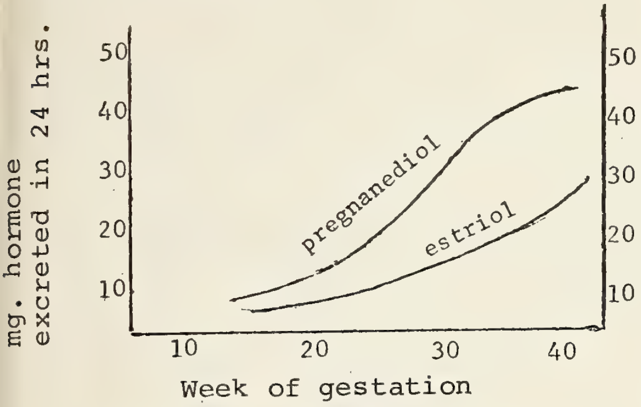

Figure 1
Placental hormone excretion during pregnancy

A number of unrelated observations appeared within the space of several years to give us considerably more insight into this disease. Since the histopathology of this disease suggests cholestasis, and since the retention of bile salts has been thought to cause the pruritus of biliary cirrhosis, two Swedish investigators, Sjövall and Sjövall, undertook in 1966 to measure serum bile salts in normal pregnant women and in six pregnant women with pruritus.[15] The mean concentration of total bile acids in the normal patients was 0.087 mg.% and for the pruritic patients 2.48 mg.%. This is almost 30-fold difference between the two groups.

Datta and Sherlock[16] had demonstrated in 1961 that pruritus associated with biliary cirrhosis could be relieved by cholestyramine and that concomitant with symptomatic improvement there was a marked increase in fecal content of bile acids. On the basis of this work, cholestyramine has been used with striking success in the treatment of hepatic dysfunction of pregnancy. Almost invariably it has been associated with partial if not complete relief of the pruritus which is highly resistant to previously employed local unctions and other standard anti-pruritics.[2, 4] To date no reports of bile acid studies before and after cholestyramine therapy are available.

Cholestyramine is a quaternary ammonium anion exchange resin which binds intestinal bile salts, thus preventing their reabsorption. However, it also binds all other substances with sterol nuclei such as the metabolites of endogenous steroid hormones. For this reason, the exact cause and effect of bile acids causing pruritus relieved by cholestyramine has not been proven, but it seems likely that some anion-exchangeable sterol is responsible.[15]

Normally 80% of bile acids reaching the intestine are reabsorbed into the enterohepatic circulation, and in the condition of cholestasis, from whatever cause, it appears they cannot be cleared again or resecreted by the liver, and thus they accumulate in blood and tissues. What is true of bile acids, in this situation, is also true of bilirubin and theoretically true for any number of resorbed steroid metabolites.

If the pruritus of this disease is due to accumulation of bile salts or other similar substances, what could be causing this dysfunction? Why might this occur during pregnancy and continue to occur every time certain patients get pregnant? It is necessary to re-examine the liver in pregnancy and to re-emphasize published observations that the function of the liver in pregnancy is not entirely normal; that is, it operates with a reduced excretory capacity.

One of the hallmarks of hepatic dysfunction of pregnancy is an elevation of the alkaline phosphatase. In fact, this test more than any other has given rise to the concept of this disease as intrahepatic cholestasis of pregnancy. However, the abnormalities of the alkaline phosphatase are quantitatively similar to those attendant on normal pregnancy. Thus, Wetstone et al[17] reported in 1958 that the mean alkaline phosphatase increased during normal pregnancy until at term the mean value was 6.9 Bodansky units with a range of 2.7 to 15.0 units. (Normal was less than 5.0 units.) Fast and Roulston in 1964[18] reported the median value of 19 King-Armstrong units in the third trimester with a range of 10 to 40 units. The source of the high alkaline phosphatase is unknown at the present time, although some authors have speculated it comes from the placenta. However, a recent review emphasizes the great difficulties involved in assigning sources and functions to the alkaline phosphatase, and the question must be considered open.[19] The point is, the main historical chemical tag of this disease may actually have little value.

The serum bilirubin in pregnancy is normal, but the ability of the pregnant liver to excrete bilirubin is not. This was demonstrated by Soffer as early as 1933.[20] The excretory reserve of the liver is sufficient that the serum level is not elevated, even though, particularly during the latter half of pregnancy, the ability to clear infused bilirubin is reduced.

In pregnancy the BSP test is normal, that is, the percent retention of bromsulfophthalein 45 minutes after the injection of 5 mg. per kilogram is normal. However, the liver's capacity to excrete BSP in the latter half of pregnancy is not normal. This ability is measured by infusing sufficient BSP to keep the serum level at 2-3 mg.% at all times and then measuring how much the liver is able to excrete. In latter pregnancy the maximum excretory capacity decreases 27%.[21]

Some observers have said that the BSP test is simply and solely a measure of hepatic blood flow, and one can imagine someone contending that during pregnancy the stress of this or the mechanical stretch of that causes a decrease in the hepatic blood flow. While no doubt the hepatic blood flow does influence the percent of BSP retention, it does seem that other factors must be of importance. During pregnancy, the liver's ability to absorb or store BSP actually increases as shown by the very convincing work of Combes et al in 1963.[21] It is unlikely this would happen if the simple flow theory obtained. Moreover, the reduction in T-max for BSP in pregnancy is reflected in an increase in conjugated as well as free BSP in the blood. Again, it seems unlikely that hepatically-conjugated BSP would increase if the blood flow had simply decreased. Apparently, at least two changes occur in the liver during pregnancy. The first is an increase in the liver's ability to absorb BSP, and the second is an impairment in the active transport mechanism that transports BSP through the hepatocyte membrane into the bile capillary.

It seems, therefore, that during normal pregnancy a change occurs which results in a decrease in the excretory capacity of the liver. In most women this decrease is so small and the excretory reserve of the liver so large that no abnormalities are noted in the serum bilirubin and the standard BSP excretion. On an empirical basis we might expect, however, that at the end of a bell-shaped curve perhaps genetically determined there would be individuals whose functional hepatic capacity is so limited that abnormalities might appear under the stress of pregnancy. Perhaps these are the individuals who suffer hepatic dysfunction of pregnancy.

In any case, the question is, what is there about pregnancy that creates a stress sufficient to constitute a disease in a small minority? The answer is not entirely known but most likely revolves around the hormones of pregnancy, estrogen and progesterone. There is already a model for steroid-induced jaundice, and that is methyltestosterone. There is a large collection of data referable to it and to what are called C-17 alkyl-substituted steroids. Many feel that the phenomenon of methyltestosterone cholestasis depends on the alkyl group substituted at carbon 17. However, abnormalities have also been demonstrated with the natural estrogens, estriol and estradiol, which do not have alkyl substitutions at carbon 17,[22] and also to a synthetic androgen devoid of C-17 substitution.[23]

Hsia et al[24] investigated the serum of pregnant women in a search for an inhibitor of glucuronyl transferase. They found significant amounts of an inhibitor of this enzyme that increased with the duration of pregnancy and fell sharply after delivery. When they fractionated serum to find the cause of this inhibition, they were able to isolate three substances, pregnanediol, 3,20 allopregnanetriol and pregnanolene. They then tested a series of 9 physiologic progestins and found inhibitions of 50% in three of them and from 15 to 36% in the remainder. These authors speculated that the high levels of these maternal hormones circulating in the newborn might inhibit the infant's own glucuronyl transferase and thus cause "physiologic" jaundice of the newborn. Glucuronyl transefase is the enzyme that conjugates bilirubin, and it is also involved in the hepatic conjugation of BSP.[25]

All of the progestins just mentioned have C-17 alkyl substituents. In 1964 Mueller and Kappas[22] infused the natural estrogens estriol and estradiol into 29 women and two men and observed a rapid and consistent impairment in hepatic excretory capacity of BSP in all but three of the patients tested. The 45-minute BSP value rose commonly to 10-15% retention and as high as 30%. Interestingly, the alkaline phosphatase also rose to abnormal levels in 50% of the patients. These abnormalities persisted as long as estrogen was administered and returned to normal almost immediately the estrogen was discontinued. Liver biopsy was performed in six of these patients and showed no abnormality. Electron microscopy was not done. Whereas it was previously thought that an alkyl substitution at carbon-17 was necessary to produce liver abnormality, this study demonstrated abnormal function induced by the natural estrogens which have no C-17 substituents.

There is one further link in this story, and that concerns the oral contraceptives. If patients with hepatic dysfunction of pregnancy are unable to tolerate their own elevated levels of hormones, it is tempting to think they could not tolerate exogenous hormones. This appears to be the case.

There are now in the literature at least 42 cases of jaundice occurring in women taking the anovulatory agents.[4] Six of these were never pregnant, and in 13 there is no obstetrical information. Of the remaining 23 who have adequately recorded histories, only six have had normal pregnancies. Five have had pruritus of pregnancy and 12 have had hepatic dysfunction of pregnancy. Thus, out of a possible 23 patients in whom this can be evaluated, over half have previously demonstrated the gross form of the disease and another five may well have had the basic dysfunction.[4] Haemmerli and Wyss thus conclude that patients who have had this disease should not take the anovulatory agents.

Discussion

Our knowledge of the etiology of this disease can be retraced in the following short observations:

1) Svanborg and Thorling established hepatic dysfunction of pregnancy as a syndrome in the 1950's.
2) The relationship of the disease to pregnancy, particularly the placenta, was shown by its abrupt termination on delivery and, in one case, by its cure after removal of retained secundines.
3) Sjövall and Sjövall showed bile acids are increased 30-fold in pregnant women with pruritus.
4) A number of investigators achieved striking relief of pruritus with the exchange resin, cholestyramine, which increases the fecal excretion of bile acids.
5) In normal pregnancy the ability of the liver to excrete bilirubin and bromsulfophthalein is significantly impaired.
6) The infusion of natural estrogens causes similar abnormalities in presumably normal females as well as males.
7) Several natural progestins are rather potent inhibitors of glucuronyl transferase.
8) This disease has been reduplicated in patients who subsequently received common anovulatory agents. These contain synthetic estrogens and progestin and have C-17 alkyl substituents.

One can speculate that the natural as well as the synthetic hormones, estrogens and progestins, contain in their common steroid nucleus a structure which interferes with the action of several excretory liver enzymes, including glucuronyl transferase. This effect might be the result of a quantitative genetic defect rather than a qualitative one. Thus, for example, two standard deviations of a given population might have 50 to 100 units of hepatic excretory function. One percent of a bell-shaped curve will have more than 100 units and one percent will have fewer than 50. Now if 40 units of function were a critical level in the development of retention of bile acids (or other offensive sterols) most individuals could lose 10 units of function from increased hormone load without becoming clinically ill. However, a critical level might be passed in a small portion of the population. By this purely hypothetical mechanism, one would not have to suppose a qualitative genetic abnormality. The size of the pool of individuals with low hepatic excretory capacity remains to be delineated. However, Topp and Bruce[10] quote Kasdon as finding pruritis in fully 13% of his presumably normal obstetrical patients. Whether or not this symptom is associated with any demonstrable abnormality is unknown. The measurement of bile acids is not commonly available, and there is no reported large-scale screening of these substances.

The exact site of hepatic dysfunction also remains unknown. The difficulty probably does not arise simply from the apparent "plugging" of bile radicals as is suggested in the term "cholestasis of pregnancy." Rather, the defect most likely resides somewhere in the hepatocyte and in its failure to excrete substances into the biliary tree. The precipitation of bile salts would then reflect a reduction of flow of excreted material through the biliary tract. An analagous situation might be in bile nephrosis where it now appears that the precipitation of bile pigments is not a pathogenetic obstructive mechanism, but rather a reflection of a marked decrease in the glomerular filtration rate.

Summary and Conclusions

The preceding paragraphs have described the clinical observations of a disease of pruritus and jaundice associated with pregnancy and almost invariably recurrent with successive pregnancies. The association of an extremely high fetal mortality rate is unexplained and belies its designation as benign jaundice of pregnancy. Independent observations have suggested that the disease is symptomatically associated with increased blood levels of the bile acids, and that an exchange resin cholestyramine is effective in treatment. A review of hepatic physiology during pregnancy emphasizes that normally the liver's excretory capacity is reduced. That this might be the result of high circulating levels of estrogen and progestins is suggested by several studies. The clinical reproduction of the disease by synthetic substances reaffirms the basic responsibility of steroid hormones in its pathogenesis. A mechanism of cholestasis is postulated to be less important than an excretory defect in the hepatocyte perhaps related to hormonal inhibition of hepatic excretory enzymes. For this reason it is proposed that the term hepatic dysfunction of pregnancy is more descriptive of this malady than the present term recurrent intrahepatic cholestasis of pregnancy. Because of a presumably constant and epidemiologically large reservior of patients, this disease may represent the best present model of drug-induced jaundice.

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Surgery For Coronary Disease

William H. Sewell, M.D.

Animal experiments were begun in 1953 in an effort to learn enough about the physiological factors that control the development of collateral channels to coronary arteries to permit the design of a consistently reliable operation for patients with coronary insufficiency. The information obtained led to the conclusion that the Vineberg mammary implant was the only one of several dozen proposed operations that could be even remotely considered to be on a sound physiological basis. There seemed, however, to be considerable room for improvement in the direction of more consistent collateral development to more areas of the heart in a higher percentage of patients.

A review of some of the earlier animal experiments was reported in *Connecticut Medicine*.[1] Recently, details of the entire series of experiments have been published.[2] The basic experiments and earlier clinical experience have led to the establishment of the current coronary program at the Guthrie Clinic. An outline of the policies being used is herein presented.

CORONARY ARTERIOGRAPHY

Reliably accurate and safe coronary arteriography is essential for any type of sound surgical approach to the treatment of coronary disease. Selective coronary cinearteriography by the Sones method[2, 3] in my opinion is the only technique proposed so far that is satisfactory for this purpose. There is good reason to believe that the accuracy level is better than 98% if, and only if, the technique recommended by Sones is followed, and filming is done with apparatus that would meet with his approval. Compromise from a 6″ to a combination 6-9″ image tube reduces the accuracy somewhat, and a 9″ tube reduces it markedly. Compromise from an overframing lens to one that gives a round picture in a white rectangle reduces the accuracy seriously. Compromise from 35 to 16 mm film reduces it moderately.

Indications for Coronary Arteriography

In theory there are three separate indications but in practice they often overlap.

Diagnostic Problem

Despite occasional claims to the contrary, I feel that the chances of error are extremely low if a definite diagnosis of coronary disease is made on the basis of an infarct proven by QRS abnormalities, or an exercise tracing showing a horizontal ST segment that is depressed 1.5 mm or more. The accuracy that can be expected in various other clinical groups is much lower and is indicated by the findings in Table I. These, in general, are in agreement with those reported by Proudfit[4] from the Cleveland Clinic series.

Problem of Management

This problem sometimes arises in a patient who is doing well after a healed infarction and wishes to know how much, if any, he should restrict his activity. Restriction does not seem necessary if he has already infarcted all areas threatened by his coronary sclerosis, or if he has developed adequate collateral around such lesions. On the other hand, restriction is advisable if he has additional tight constrictions threatening further infarction.

Surgical Candidate

A surgical candidate must be free of clinical contraindications for the pedicle operation, and must be either sufficiently disabled by symptoms of coronary disease or sufficiently worried about dying of this disease to be interested in major surgery. This group, therefore, can include patients who are asymptomatic after an infarction.

Contraindications to Arteriography

Mason Sones has been heard to comment that coronary arteriography can be performed safely on any patient who "can walk through the door and lie down on the table." Although occasionally successfully performed, arteriography is not recommended on patients who are too orthopneic to lie flat or those who are not ambulatory. The only additional contraindication that we accept is frequent episodes of paroxysmal atrial tachycardia or ventricular tachycardia. The most common contraindication is lack of an indication, for example a sedentary patient with proven diagnosis who could not have surgery or does not want it no matter what the arteriographic findings turned out to be.

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TABLE I

CORONARY ARTERIOGRAPHIC VERSUS CLINICAL FINDINGS

	No Definite History of Infarction			*Definite History of Infarction*		
Arteriographic Findings	*Typical Angina*	*Atypical Angina*	*No Angina*	*Typical Angina*	*Atypical Angina*	*No Angina*
Normal	8	32	9	1	3	1
Normal To ½ Normal Diameter Open	—	3	1	—	—	—
½ To ¼ Normal Diameter Open	—	2	2	1	1	1
Less Than ¼ Normal Diameter Open	15	14	2	20	10	5
Occlusion	33	10	1	21	15	20
Technically Inadequate	1	2	—	—	2	—
Total	57	63	15	43	31	27

Risks of Arteriography

Sones has stated that properly performed coronary arteriography should carry a mortality risk of less than 1 per 1,000. So far, I personally have performed 509 arteriograms with no mortality or significant myocardial infarction.

Loss of the radial pulse as a result of brachial occlusion is not a disasterous complication but usually gives annoying symptoms for several months. This was a common occurrence initially, but has happened only twice in the 236 cases done at this institution.

Failure to get a complete study is the most common complication. No useful information was obtained on 5 of the 236 patients in the current series. The description of one or more coronary branches was equivocated for one reason or another in an additional 47 patients.

Arteriographic Findings

The findings of the 236 patients done at this institution are presented in Table I.

Of particular interest is the finding of no coronary obstruction in 14% of the patients with typical angina and no history of infarction. Those with atypical angina had a much higher likelihood of normal coronary arteries, but 38% had severe and dangerous coronary disease. The 9 patients with history of neither infarction nor angina were referred because of suspicious ECG findings or a strong family history of premature coronary disease. Three had dangerous constrictions.

The group with post infarction typical angina had serious coronary constrictions in 95%, which is the highest of any group. It is to be noted, however, that 5% of the patients referred with an unequivocal history of myocardial infarction had normal coronary arteries. In none of these were QRS complexes found to be outside normal limits.

SIGNIFICANCE OF THE ARTERIOGRAPHIC FINDINGS

There is no valid reason to think that spasm in a normal coronary artery (unless obstructed by a catheter tip) gives symptoms, leads to complications, or requires treatment.

Constrictions leaving between ½ and ¼ of the normal lumen diameter open are definitely capable of causing angina, leading to infarction, or causing sudden arrhythmic death. However, many and perhaps most of the constrictions in this range are asymptomatic. Surgery is not indicated in this group. Medical management is definitely indicated and can be expected to give good results.

Constrictions leaving less than ¼ of the original lumen diameter still open that are not compensated by intercoronary collateral channels and involve the majority of the arterial supply to one or more of the three aspects of the left ventricle can also lead to the above complications. Medical management is well worthwhile in this group but cannot be expected to be entirely adequate. Surgery, therefore, is worthwhile if not contraindicated.

THE MEDICAL MANAGEMENT

In general, conventional indications for most cardiac drugs are accepted. Anticoagulant drugs are not used for coronary disease in ambulatory patients.

The Nitrate Regimen

The nitrates used are nitroglycerin, sublingual Isordil, and the Isordil Tembid. The pertinent pharmacological effects have been carefully reviewed.[2]

Nitroglycerin is the strongest of the coronary vasodilating drugs. It increases the flow through collateral channels to ischemic areas of myocardium and relieves spasm if present. It may decrease the peripheral resistance in the coronary arterial tree and also lower aortic pressure, giving the heart less work to do and sometimes more myocardial perfusion. The effect on collateral channels lasts about 10 minutes, and that on the arteriolar resistance is over less than a minute after it is last added to the bloodstream.

Sublingual Isordil has the same effects as the nitroglycerin, but is less potent. However, the increase in flow through collateral channels persists for about two hours. The effect on the capillaries is probably over within a few minutes.

The Isordil Tembid does not give maximal dilation of coronaries but, in my opinion, discourages the development of coronary spasm and encourages the development of collateral channels to coronary arteries.

Results

There are 55 patients in the group who have one or more constrictions leaving less than ½ the lumen diameter open but do not have enough coronary constriction (or else already have too much collateral) to give an indication for surgery. Thirty-six of these patients have been followed for a total of 448 patient months. So far, there has been one infarction and no coronary deaths in this group.

There are 107 patients in the group with sufficient coronary constriction to give an indication for surgery. A total of 367 out-patient months during which there was no reasonable probability of protection from the pedicle were accumulated by the patients in this group. There were 2 infarctions sufficiently severe to alter the QRS complex. There was a total of 709 patient months with proven or presumed collateral from the pedicle accumulated altogether. There was 1 infarct in this group.

A control series for the above groups is not available. However, we know that these patients all had arteriographically proven severe coronary arterial disease. Table I shows that they represent the most severe end of the coronary spectrum. If we would expect one infarct every two years in such a patient, then a total of 30 infarctions should have occurred instead of the 1 that was actually observed. If this estimate is in error and we would expect one infarct every four years in a control series, then 15 would be expected. The observed results still are most encouraging.

SURGERY

Choice of Procedure

The triple pedicle is the only procedure being currently performed at the Guthrie Clinic for coronary disease. In theory, Effler's endarterotomy and patch-graft[5] would be the procedure of choice if surgery is to be done for a patient with coronary symptoms caused by a localized lesion in the midportion of the right coronary with an entirely normal coronary tree. So far, such a patient has not been personally encountered.

Indications for Surgery

Surgery is not indicated unless demand for collateral exists. Demand is considered to be present if all or the majority of the arteries to one of the three aspects of the left ventricle are constricted tightly enough to leave less than ¼ of the normal lumen diameter open, and there is no compensating intercoronary collateral channel or prospect of one developing.

Surgery is indicated if there is demand in two or three of the three aspects of the left ventricle, whether the patient is symptomatic or not. It is indicated for demand in a single aspect with no intercoronary collateral, but not if a collateral is present since such patients do well on medical management.

Contraindications for Surgery

Surgery is not considered in patients with an estimated physiological age of over about 65. Clinical contraindications include conditions that would make thoracotomy risky, such as emphysema, severe hypertension, renal disease, or severe diabetes. Patients weighing more than 20 pounds above ideal weight or refusing to stop smoking despite a productive cough are considered to have relative contraindications.

A patient with surgical demand in all three aspects of the left ventricle is not considered to meet a contraindication if the end diastolic pressure in his left ventricle is below 15 mm Hg. Likewise, a patient with an end diastolic pressure over 14 mm Hg but who has less than surgical demand in one of the aspects of the heart is accepted. However, a patient with both unfavorable factors against him despite optimal medical management is considered to have an absolute contraindication to surgery.

The frequency of indications and contraindications to surgery in the arteriographic series is shown in Table II.

TABLE II

INCIDENCE OF INDICATIONS AND CONTRAINDICATIONS FOR SURGERY

No Significant Coronary Disease	58
Medical Treatment Only	55
Surgery Indicated	107
Surgery Contraindicated Arteriographically	7
Surgery Contraindicated Clinically	4
Technically Inadequate Arteriograms	5
Total	236

Surgical Technique

The triple pedicle is made from the internal mammary artery, mammary vein, adjacent muscle, and connective tissue. It includes also the 4th and 5th or 5th and 6th intercostal arteries which are allowed to remain attached to the mammary artery anteriorly. The technique for surgery has been described in some detail.[2]

Limbs can be placed in the anterior, lateral, and posterior aspects of the left ventricle. If a patient has double disease, then the third limb is placed in the area most likely to need two implants. The most common pattern consists of separate constrictions involving the anterior descending, the diagonal branch, and the left marginal coronary arteries. The procedure usually takes 2½ to 3 hours skin to skin, and the blood loss averages about 300 cc.

Operative Mortality

There have been 106 pedicle operations performed at this institution. The following data includes also the 134 pedicle patients previously reported.[2]

The operative mortality is given in Table III. There was one hospital death during the most recent 38 consecutive cases.

TABLE III

OPERATIVE MORTALITY

	Single Pedicle	*Multiple Pedicle*	*Total*
Triple Disease and Elevated End Diastolic Pressure	6/7	1/2	7/9 (78%)
Triple Disease with Normal End Diastolic Pressure	0/18	4/45	4/63 (6.3%)
Less Than Triple Disease	3/79	1/89	4/168 (2.4%)
Total	9/104 (8.7%)	6/136 (4.4%)	15/240 (6.2%)

Evaluation of Results

In my opinion, selective mammary cinearteriography is the only satisfactory method of those so far proposed for evaluating the development of collateral to the coronary arteries from an implanted vessel.[2] It alone demonstrates the size, location, and number of collateral channels; the direction and velocity of movement of blood through them; and the destination of this blood. Work by Gorlin's group[6] strongly supports the concept that sufficiently good collateral channels to permit opacification of coronary arteries can be expected to reverse an ischemic lactate production to a normal pattern, meaning that the pedicle has given metabolic improvement.

Mere patency of the implant is not associated with improvement in the myocardial metabolism, and in my opinion does not mean that a successful result was obtained. Patency rates, therefore, should not be accepted as indicative of the success rate of the technique.

Although postmortem arteriography might demonstrate the existence of collateral channels, it does not tell whether or not sufficient blood passed through them during life to be of any significance. Such studies, therefore, are misleading and again should not be accepted as evidence of the success of an implant.

A randomized medical control series has been proposed and to some critics appears to be the ideal control. Actually, such a study could be rather misleading. Failure of the surgical group to show an improvement in infarction and longevity rate would mean only that the surgery as performed was of no value. Only if accompanied by arteriographic demonstration of coronary filling through collateral from the implant would such a study cast doubt upon the ability of such collateral to prolong life, since survival of a patient after such an implant by no means guarantees that collateral will develop. On the other hand, an improved longevity or infarction rate in such a surgical group would not prove that the surgery was of physiological benefit, unless accompanied by arteriographic demonstration of collateral, because the confidence gained from a supposedly worthwhile operation could actually influence the infarction rate.

The only satisfactory control, therefore, is the unintentional equivalent of a "sham operation." This group consists of the patients who have had the operation but who are found arteriographically not to have satisfactory collateral. It is true that individual variations in the disease might affect the collateral development. However, those with the more severe disease would have stronger demand for collateral and such an effect should work against the surgeon instead of in his favor. This means that a better infarction or mortality rate in those demonstrated to have collateral can be presumably credited to the operation.

MAMMARY ARTERIOGRAPHIC RESULTS

Mammary arteriography was performed on 148 of the 156 patients that survived the first postoperative year after a pedicle operation. Of these, technically successful studies were obtained on 143. Retrospectively, 11 of the patients did not have an implant in an area of demand, either because of failure to understand what demand consisted of early in the series, errors resulting from the use of a 9″ image intensification tube, or failure to identify coronary branches accurately in the operating room.

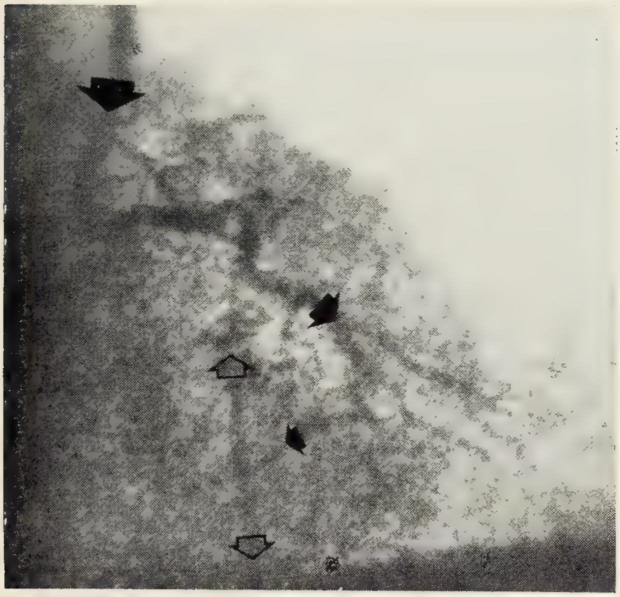

Figure 1

A single frame from a selective mammary cinearteriogram taken approximately 12 months postoperatively. The mammary artery is well opacified and can be followed down the sternum (large solid arrow). It turns to the left as it becomes pedicle. It courses downward and to the left (medium solid arrow) where it gives intercostal branches. The distal mammary limb (small solid arrow) gives good collateral to the anterior descending which fills retrogradely and distally (open arrows). (PA Projection)

This leaves 132 patients suitable for analysis. These results are presented in Table IV. Table V gives the criteria used for rating the mammary arteriograms in Table IV. Each limb of a multiple pedicle is rated separately and added together giving a theoretical maximum of 15 for a triple pedicle. The only exception to the arithmetical addition is that a grade I result is not considered to add any blood to the myocardium and, therefore, is omitted from the addition. The table shows that a patient, therefore, had a 92% chance of getting a 3+ or better rating with the triple pedicle being currently used.

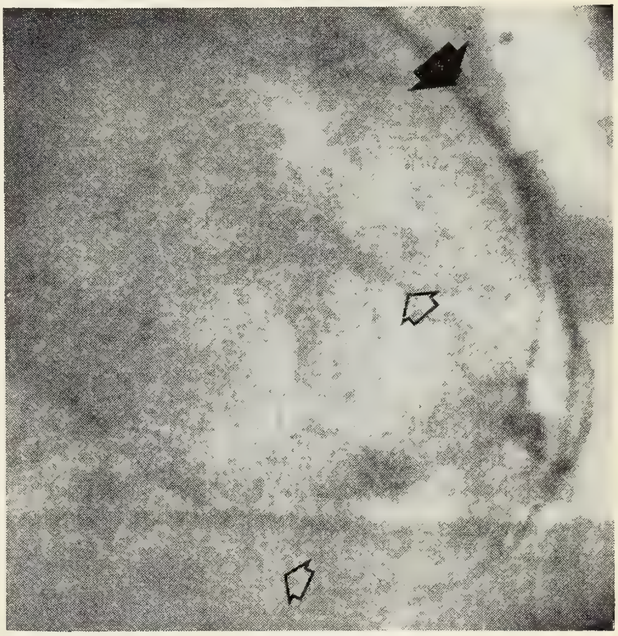

Figure 2

A similar frame from another case. The mammary artery in the pedicle (solid arrow) gives three branches which may be seen individually. There is opacification of the left marginal (upper open arrow) and faint opacification of the posterior descending (lower open arrow). The third limb did not give sufficient collateral to opacify a coronary branch. (PA Projection)

Late Mortality

Table VI shows the mortality after completion of the admission for the pedicle operation. It averages about 1% per month for the first six months, which is probably about the mortality to be expected from the disease being treated on the medi-

TABLE IV

NUMBER OF PATIENTS WITH EACH MAMMARY ARTERIOGRAPHIC RATING

	0	*1+*	*2+*	*3+*	*4+*	*5+*	*6+*	*7+*	*8+*	*9+*	*10+*	*11+*	*12+*	*13+*	*Total*
Single Pedicles	0	5	14	7	17	26	—	—	—	—	—	—	—	—	69
Double Pedicles	0	0	3	5	2	6	1	3	3	1	5	—	—	—	29
Triple Pedicles	0	0	2	0	1	4	1	6	8	2	4	1	2	3	34

cal regimen that is being used. The later decrease in mortality is encouraging.

TABLE V

CRITERIA FOR MAMMARY ARTERIOGRAPHIC RATING

0	Mammary Occluded
1+	Mammary Patent Only
2+	Opacification of Small Coronary Arteries
3+	Opacification of Large Coronary Arteries
4+	Faint Venous Opacification
5+	Dense Venous Opacification

TABLE VI

EARLY POSTOPERATIVE CORONARY MORTALITY

Time Period	*Patients Entering Period*	*Deaths During Period*	*Percent*
2 Wks.- 6 Mos.	230	14	6.1%
7 Mos.-12 Mos.	189	6	3.2%
13 Mos.-18 Mos.	157	2	1.3%

This table shows the mortality that presumably occurs in spite of the operation but not because of it. At first glance, some of the figures may not appear to add up properly. This is because the more recent postoperative patients are still within a given time period.

Table VII shows the deaths that occurred after the mammary arteriograhic rating was available. There is a decided trend toward a lower mortality in those with good arteriographic ratings. The majority of the poor results were obtained early in the series. The differences, therefore, are not quite as marked when the death rate is corrected for patient months of observation. Nevertheless, the trend is still quite encouraging.

TABLE VII

MAMMARY ARTERIOGRAPHIC FINDINGS VERSUS PATIENT SURVIVAL

Mammary Arteriogram Rating	*Deaths/ Pts.*	*Deaths/ Pt. Mos. Since Arteriogram*	*Pt. Months/ Death*
0, 1+	2/8	2/140	70
2+	2/15	2/242	121
3+ or More (Single Pedicle)	4/50	4/668	167
2+, 3+, 4+ (Multiple Pedicle)	1/15	1/106	106
5+ or More (Multiple Pedicle)	1/48	1/315	315

Clinical Results

The clinical result is quite important to the patient and to the referring physician. An observer who personally sees the patient usually can tell quite easily whether there has been clinical improvement because it is quite clear cut in most patients with good arteriographic results. Improvement from grade 3 or 4 angina to grade 1 or 0 angina is not uncommon. Unfortunately, clinical rating by one observer cannot be compared to that by another, and a percentage of patients improved cannot be used as a basis for the valid comparison of operations for coronary disease.

It is sufficient to say that the majority but not all of the patients with a good arteriographic result get a good clinical result and vice versa. Progression of coronary disease can neutralize a physiologically effective pedicle. On the other hand, development of intercoronary collateral channels can give physiological and clinical improvement that might be erroneously attributed to a poorly functioning pedicle. Psychological factors can work in either direction.

The placebo effect of surgery is often profound but can usually be distinguished from the physiological effect. It comes on promptly postoperatively. It may persist or wear off but does not increase after the second postoperative month. On the other hand, physiological effect can be expected to manifest itself in clinical improvement beginning about two months postoperatively and continuing for one to two years before leveling off.

FUTURE GOALS

The obvious goal of a triple pedicle operation is the establishment of grade 5 collateral to all ischemic areas of the hearts of all patients within the first year postoperatively. Technical refinements are being made in an effort to more closely approach this goal. Considerable progress is expected during the next year or two.

The current operative mortality of 4.4% and the 3% rejection rate because of too far advanced coronary disease does not leave much room for improvement in these directions, though safe inclusion of patients over 65 is a challenge.

There is every reason to expect that the current trends will continue and hopefully within the next few years the statistics will be sufficiently convincing to permit a claim of demonstration of the value of the operation on a statistically significant basis.

SUMMARY

In the series presented, coronary disease is managed according to the findings in Sones type selective coronary arteriography. Twenty-five per cent of the 236 patients in the arteriographic series were found to have no significant coronary obstruction. Twenty-three per cent had sufficient constriction

to require medical management but not enough to indicate surgery. So far, the management has been completely adequate for prevention of complications in this group.

Forty-five per cent had sufficient constriction to indicate surgery in addition to the medical regimen. Only 3% were rejected because of too much coronary disease. Two per cent had clinical contraindications to surgery and 2% had technically inadequate arteriograms.

The operative mortality was 8.7% of the 104 single pedicles, and 4.4% of the 136 multiple pedicles. The mortality rate during the first six postoperative months was 6.3% and fell to 3.7% during the next six months.

Mammary arteriography is considered the only valid method for assessing the development of collateral from the pedicle. Mere patency of the implant or postmortem demonstration of collateral channels is not satisfactory and a randomized medical control series would probably be misleading.

Mammary arteriography was done on 95% of the 156 pedicle patients that survived the first postoperative year. Of these, 132 are suitable for analysis. Enough collateral to be considered at least minimally successful was demonstrated in 72% of the single pedicle patients and after 92% of the multiple pedicles.

There was one coronary death per 70 patient months among those with no collateral, per 121 months among those with minimal collateral, per 167 months among those with good collateral from single pedicles, and there has been one death during the 315 patient months accumulated by patients with good collateral from multiple pedicles.

The incidence of good collateral to multiple areas of the heart after the triple pedicle appears to be considerably better than that claimed for any other procedure so far.

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Differences Between Speaking And Writing

Speaking is an art in itself. The temptation to use an article, perhaps already in the press, as text for a talk should be resisted; it is better to plan the communication afresh. A speech should be looser in texture than the script of an article. The listener has to accept the speed chosen by the speaker, whereas the reader can choose his own pace, lingering over obscure passages or skipping quickly over pieces of lesser interest and importance. In listening, continuous attention is needed; there is no time to pause or to study an illustration again. So the speaker must speak clearly and simply, and perhaps repeat key points. No one wants to hear a speaker "talking like a book".—Hawkins, C. F. and Hammersley, D. P.: Speaking at Meetings, *Med Biol Illus* 16:229 (Oct) 1966.

THE PRESIDENT'S PAGE

This is the "season to be jolly". We read this message many times daily in every conceivable medium, and those who can't read, hear it from every mercantile establishment. Indeed, the plethora of such pronouncements is often so abundant as to make many of us just a little disgruntled. We sometimes feel that Christmas has become some sort of a carnival, promoted by the retail stores in order to sell more goods.

Certainly, we have to search to find the real significance of the Christmas season. In essence, it is the story of the birth of Christianity. It celebrates an event which truly changed the world, and continues to have a deep effect on every living person regardless of religious belief.

The sublimation of the true Christmas story under the more material aspects of the season need give us no cause for dismay. At no other time of the year are people quite so considerate. It seems that all the polite phrases come readily to the lips during this period. It is difficult to provoke an angry word. There is a hopeful attitude which is so apparent to all who look. The whole world seems to be pervaded by this feeling of good will.

Many doctors feel we have little to be pleased about this year. We are indeed beset by forces which some find it difficult to understand. It seems to us that we are in danger of becoming part of a huge system of socialism which is repugnant to us and which we know will cause a deterioration in good medical care. People with no medical background are telling us what should be done to improve medical care, and in many instances, their ideas run contrary to what we know is needed. We should all know that good medical care will come out of all this confusion in the end, for we are dedicated men who place sound medical care above all else.

Christmas is the time for giving and not for receiving. No one can really know the meaning and the thrill of Christmas until he gets into the joy of giving and forgets his own desires. To see someone's face light up with pleasure is worth more than any gift. Since this is so, the doctors are in a splendid position to enjoy the season. We bring gifts which are really priceless and part of ourselves. We bring the very breath of life. We bring relief of pain and suffering and above all else we bring compassion and understanding. Rare gifts indeed.

So, Merry Christmas Doctor, to you and yours.

Norman H. Gardner, M.D.

If you think the pink pill for U.R.I. symptoms is built for speed and endurance you're on the right track.

Here is a tablet that begins to relieve symptoms of upper respiratory infection quickly—a tablet that works for hours to make it easy for your patient to enjoy continuous relief.

Novahistine Singlet combines effective dosage of an antipyretic-analgesic with a vasoconstrictor-antihistamine formulation to relieve not only the congestion, but also the fever and the aches and pains that almost always accompany upper respiratory infections.

A total daily dosage of 3 or 4 tablets will normally provide the continuous relief your patient expects. Use with caution in patients with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result.

PITMAN-MOORE Division of
The Dow Chemical Company,
Indianapolis, Indiana.

Novahistine® Singlet decongestant-analgesic

(Each tablet contains: phenylephrine hydrochloride, 40 mg.; chlorpheniramine maleate, 8 mg.; acetaminophen, 500 mg.)

DOW

Special Article

Smoking Attitudes of New Haven County Physicians: A Survey

Ned Thomas

The general public seems not to have heeded the warning in the Surgeon General's report on cigarette smoking except for a brief period after it was released in 1964.[1] We wondered what effect it has had, if any, on Physicians attitudes towards cigarette smoking. If physicians changed their attitudes, by giving up the cigarette habit, then it could more readily affect the thinking, attitudes, and practices of their smoking patients and utlimately the general public.

With this in mind we succeeded in interesting Robert L. Leeney, executive editor of the Register, and officials of the New Haven County Medical Association, who also agreed to a survey of the New Haven County Physicians. Dr. Hyman Levin, the secretary, kindly furnished the roster of the County Physicians. The questions (Table 1) required answers of yes or no, no identifying signatures, and were sent out with a stamped self-addressed envelope. In addition to the County membership a somewhat enlarged questionnaire was also addressed to faculty members at the Yale Medical Center, (Table II).

The final sponsorship besides the Register, the New Haven County Medical Society and Dean Frederick C. Redlich of Yale, also included the New Haven Chapter of the American Cancer Society whose volunteers collated the results of the survey.

TABLE I

A total of 743 physicians in the New Haven County Medical Association responded to the questionnaire sent out to 1025 doctors, for a 72.5 per cent response.

Questions	*# Responding*	*#*	*Percentage*	*#*	*Percentage*
1. Do you now smoke cigarettes?	743	126	(17%)	617	(83%)
2. Do you now smoke fewer cigarettes than you used to as a result of the Surgeon General's report on smoking?	351	128	(37%)	222	(63%)
3. Have you stopped smoking?	575	314	(55%)	261	(45%)
4. Have you ever smoked?	739	601	(81%)	138	(19%)
5. Have you tried to stop smoking, but been unable to?	472	84	(18%)	388	(82%)
6. Would you give up smoking if you could?	369	177	(48%)	192	(52%)
7. If you have stopped smoking, was it because you felt it was harmful to your health?	669	358	(54%)	311	(46%)
8. If you have smoked and have given it up, do you feel and better now as a result of it?	669	290	(43%)	379	(57%)
9. If you smoked cigarettes and have given them up, do you now smoke a pipe or cigars instead?	445	140	(31%)	305	(69%)
10. Are you convinced that smoking cigarettes is as dangerous to one's health as the Surgeon General's report indicates?	725	641	(88%)	84	(12%)
11. If you smoke, do you feel inhibited about telling your patients to stop smoking?	287	49	(17%)	238	(83%)
12. Do you think that those of your patients who smoke would be in much better health if they did not?	683	643	(94%)	40	(6%)

Results

Table 1 shows the questions submitted to 1025 physicians of the New Haven County Medical Society. Of those 743 replies were filled out by the

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MR. NED THOMAS is a science medical writer for the New Haven Register and recipient of two awards from the Connecticut State Medical Society for feature writing, one in 1966 and one in 1968.

TABLE II

A TOTAL OF 134 PHYSICIANS AT THE YALE-NEW HAVEN MEDICAL CENTER RESPONDED TO THE QUESTIONNAIRE.

Questions	*# Responding*	#	*Percentage*	#	*Percentage*
1. Do you now smoke cigarettes?	133	33	(25%)	100	(75%)
2. Do you now smoke fewer cigarettes than you used to as a result of the Surgeon General's report on smoking?	80	27	(34%)	53	(66%)
3. Have you stopped smoking?	100	42	(42%)	58	(58%)
4. Have you ever smoked?	134	116	(87%)	18	(13%)
5. Have you tried to stop smoking, but been unable to?	88	22	(25%)	66	(75%)
6. Would you give up smoking if you could?	62	43	(69%)	19	(31%)
7. If you have stopped smoking, was it because you felt it was harmful to your health?	70	52	(74%)	18	(26%)
8. If you have smoked and have given it up, do you feel any better now as a result of it?	48	34	(71%)	14	(29%)
9. If you smoked cigarettes and have given them up, do you now smoke a pipe or cigars instead?	63	27	(43%)	36	(57%)
10. Are you convinced that smoking cigarettes is as dangerous to one's health as the Surgeon General's report indicates?	132	120	(91%)	12	(9%)
11. If you smoke, do you feel inhibited about telling your patients to stop smoking?	70	14	(20%)	56	(80%)
12. Do you think that those of your patients who smoke would be in much better health if they did not?	120	110	(92%)	10	(8%)
13. Do you favor restraints on tobacco advertising?	130	115	(88%)	15	(12%)
14. Do you recommend that your patients give up smoking, even if there is no obvious immediate danger to their health?	125	103	(82%)	22	(18%)
15. (a) Do you take the initiative in asking your patients to stop smoking?	121	70	(58%)	51	(42%)
15. (b) Or, do you wait until they broach the subject with you?	87	54	(62%)	33	(38%)
16. Do you think people in the health field—and possibly the government—ought to take a more aggressive approach to get people to stop smoking?	129	113	(88%)	16	(12%)
17. Do you feel the anti-smoking campaign in the U.S. is failing because:					
(a) It has not been effectively launched?	113	76	(67%)	37	(33%)
(b) The public regards the effects of smoking as "too remote" to worry about?	123	107	(87%)	16	(13%)

physicians and mailed back, amounting to a 72.5% response, which based on the results of similar surveys[3, 4] is an unusually high return. It can be seen that 4 out of 5 (83%) of those responding to the survey indicated they do not smoke cigarettes now. By contrast the percentage of physicians who formerly smoked cigarettes was 81%. This is the highest percentage of any group of doctors who do not now smoke cigarettes.

Over half of the physicians that stopped smoking cigarettes did it because they were convinced it was harmful to their health and most of these stated they actually felt better physically after giving up the smoking habit. In fact 88% are convinced that smoking cigarettes is dangerous to one's health. Practically all of the physicians think that those of their patients who smoke cigarettes would be in much better health if they did not smoke. Furthermore of the physicians who still smoke, 83% do not feel inhibited on this account from urging their patients to stop smoking cigarettes when the patient's health requires it. About one-third of physicians who gave up smoking cigarettes switched to a pipe or cigars because they do not inhale this smoke.

In a separate but similar survey (Table 11) of a group of 134 faculty members of the Yale-New Haven Medical Center, 75% of those surveyed said they do not smoke cigarettes now. In addition to the questions asked of the New Haven County physicians those at the Medical Center were asked several additional questions. It is to be noted that the responses to the questions in both groups were quite similar with several relatively minor differences. Apparently more physicians at the Medical Center were unable to stop smoking as compared to the physicians in practice (69% compared to 48%). On the otherhand more physicians at the Medical Center (20%) gave up smoking because they believed it was harmful to their health. More physicians at the Medical Center felt better after giving up smoking than did the physicians in practice (71% compared to 43%). Finally more physicians at the Medical Center switched to pipes or cigars than did the County Physicians (43% and 31%). Although 82% of the physicians surveyed at the Medical Center would recommend to their patients to give up smoking in the absence of any immediate medical requirement, a substantial number wait until the patients broach the subject before advising them against smoking.

A large majority of physicians recognize the importance of the seductive nature of cigarette advertising upon the younger generation and would favor some restraints upon this aspect of influencing the public to smoke. They would favor that people in the health field as well as government should more aggresively seek to influence the public about the health hazard of cigarette smoking particularly because the anti-smoking campaigns in this country have been feeble and ineffective. Some physicians believe the tobacco lobby "is very powerful and able to buy votes" and that a number of states oppose cigarette regulation because they depend on tobacco as a major source of revenue. The public as usual have not come to realize that the effects of smoking though often delayed should be understood as something to "really worry about."

It is interesting to note the reactions to smoking which some of the respondents volunteered. One physician who gave up smoking 1½ packs of cigarettes a day 5 years ago states "nothing grieves me more than to see healthy young people take up this habit. I think advertising commercials and everything being done to make cigarette smoking look attractive and "in" are vicious and "inexcusable". Another physician writes "many of my patients would be better off if they did not smoke and had not smoked in the past. Those with carcinoma of the lung and pulmonary emphysema came to mind immediately". The well known fact of the relation of cigarette smoking to lung disease and vascular disease are fully recognized in most personal responses by physicians.

Physicians who tried repeatedly to stop smoking but could not, frankly stated that most people "do not know how to stop smoking" and wondered if some form of group therapy might not be useful. Some recognized the addiction to smoking is very difficult to overcome and thought that safer alternatives should be looked for. Some complained that many hospitals permit smoking by patients, personnel and visitors even though these institutions are supposed to be health centers and smoking is seriously detrimental to health. The main reason one physician cited for giving up smoking cigarettes is that he wanted "to set an example" or his children. The survey shows however that there are still some physicians who believe that not all patients show ill effects from smoking.

Discussion

One of the consequences of the Surgeon General's report in 1964[1] was the stimulation of research bearing on the effect of smoking. The most striking finding is that the life expectancy is significantly shortened while invalidism occurs sooner also. The 1964 report evidently has influenced also the smoking habits of physicians. At one time many of them were heavy smokers. A recent report indicates that 100,000 physicians have stopped smoking cigarettes. Of all the physicians surveyed 35% had never smoked, 36½ had smoked at one time but had stopped and only 29% were still smoking. In contrast 52% of the general adult male population currently smoked cigarettes[3]

Other surveys indicate that physicians are deeply concerned over the effects of smoking. More than 90% stated that they associate smoking with chronic bronchitis, lung cancer, emphysema, peripheral vascular disease and coronary heart disease. The responses of physicians who have stopped smoking are also revealing. When asked in the survey questionnaire why they stopped smoking 60% checked "protect my future health", and 47% checked "occurrence of certain symptoms", and 43% checked "scientific reports". One can recognize from statements of physicians in the present survey the close parallelism of their attitudes to the other surveys and in addition their concern about methods to prevent the spread of the noxious habit and the power of the tobacco industry to frustrate these efforts. The tobacco industry has many friends in government and it spends more than 300 million annually in advertising.

It is a truism that smoking could be most effectively curbed if people did not start. It is estimated at present that over 4000 children become victims every day. Certainly many would not start if an attractive smoking image were not pressed upon them. Teenagers among whom the habit begins indicated in another survey[4] that 91½ already believe that smoking is harmful, while only 4% believe it is not. Only 2.6% of the entire sample said they definitely expect to become cigarette smokers 5 years from now, while 45.1% said they do not expect to be smokers. Another 12.3% said they probably will be smokers, while 34.2% said they probably will not be. Clearly the attitude of physicians as it is changing can have a great impact upon the prospective victims of smoking among teenagers by encouraging patients and their children to do as the physician is doing, for we now know that to stop smoking and especially not to begin the habit is to curb lung cancer, emphysema and some forms of heart disease.

Remarks by Dr. Raymond Yesner

The efforts of organized medicine, especially the American Cancer Society and the American Thoracic Society, and the concern of government, led to the Surgeon General's report on Health and Smoking in 1964, and to the requirement that a mild warning be printed on cigarette packages. If anyone was deluded that these caveats would have a lasting effect upon the smoking habits of the American public, despite the intense and pervasive seduction of tobacco advertising, he must by now be convinced to the contrary.

But one group is apparently convinced—physicians themselves! Evidence for this has been in existence for some time. The Massachusetts Medical Society reported that a third of its physicians had given up smoking. More recently a report from New Zealand indicated that 60% of its physicians did not smoke. The most astonishing evidence is the smoking habits of the New Haven County Medical Association. Almost three-quarters of the physicians returned their questionnaires, a tribute to their interest and to the credibility of the results. To the most important question, "do you now smoke cigarettes?", 83% said no. More than four-fifths of this knowledgeable group, which daily deals with the problems of health and smoking, do not smoke cigarettes. An even larger group (88%) said they were convinced that smoking cigarettes is as dangerous to one's health as the Surgeon General's report indicated. Yet only a little more than half of the physicians who stopped smoking said they did so because it was harmful to their health. For what other reason did they stop? To set a good example for their children? Their patients? Although 94% said they thought their patients who smoked would be in much better health if they did not, the physicians who continued to smoke were rather truculent about it, 83% of them maintaining they did not feel inhibited about telling their patients to stop. Still, a quarter of this group said they had tried to give up smoking, but were unable to (hard-core addicts), and more than two-thirds said they would give up smoking if they could. Of those who formerly smoked cigarettes for whatever reason (habit, pleasure, tranquilization, etc.), one-third have taken up pipe and cigar smoking as an alternative, feeling compelled to continue smoking in another and probably less harmful form. About 90% of the physicians believe the government should take a more aggressive attitude to get people to stop smoking, since the public regards the effects of smoking as too remote to worry about. This much is clear as a group the New Haven County physicians are convinced of the harmful effects of cigarette smoking, and individually most of them do not now smoke cigarettes.

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Title XIX Medical Advisory Committee Reviews Medical Claims and Utilization

In order that physicians may more effectively participate in the Medical Assistance Program (Title XIX) it is important that they know about the duties and responsibilities of the Medical Advisory Committee of the State Welfare Commissioner.

The Medical Assistance Program, commonly known as Medicaid, is a system of financing the payment of medical care for the categorically indigent and other persons who are eligible for medical assistance under terms established by the State Welfare Department.

The Medical Advisory Committee was authorized by Public Act 548 (1967 Session of the General Assembly). Its assignment is to "assist the Welfare Commissioner and his department in reviewing all claims for payment in which doubt or dispute is raised by any party to the medical assistance program and by making recommendations to the Welfare Commissioner concerning such claims."

The Act further stipulates that, in unresolved cases, or upon specific request (of the physician, patient, or third party payor), the Committee shall seek the opinion of the component county medical association in which the service was rendered.

Members of the all-physician Committee, by county, are: Hartford, Charles Polivy, Chairman; John Basile, Sidney L. Cramer, Walter Kosar, Irving Krall; Fairfield, Philip Corso, Frederick Webber, Eugene Corley; New Haven, Frank Abbot, Bernard A. Burnham, Stephen Fleck; Litchfield, Joseph McCarthy; Middlesex, Richard Grant, Andrew Turano; New London, John F. Brosnan; Tolland, William L. Williams; Windham, Romain Goyette.

Institutional members are: Frederick C. Redlich, Dean, Yale University School of Medicine; John Patterson, Dean, University of Connecticut School of Medicine; Franklin H. Foote, State Commissioner of Health; Wilfred Bloomberg, State Commissioner of Mental Health; Kenneth F. Brandon, Medical Director, Aetna Life and Casualty Company; Alan Dun, Medical Director, The Travelers Insurance Companies; E. Stuart McCleary, Assistant Medical Director, Connecticut General Life Insurance Company; and Edward M. Cohart, Winslow Professor of Public Health, Yale University School of Medicine.

The Committee was appointed by Welfare Commissioner Bernard A. Shapiro in January, 1968. Fifteen of these are practicing physicians who were selected from a list of nominees submitted by the Connecticut State Medical Society; eight other physicians were added by the Commissioner. It has since met regularly for the purpose of planning as well as assisting the Commissioner and the Department's Medical Director with policy matters and for claims and utilization review.

For efficiency of operation and proper distribution of the work load, the Committee has formed an Executive Committee, a Subcommittee on Planning, and a Subcommittee on Utilization and Review.

Executive Committee members are Dr. Polivy, Chairman; Dr. Cramer, Vice Chairman; Dean Patterson, Dr. Basile, Dr. Kosar, Dr. Corley, and Dr. Orvan W. Hess, Medical Director of the State Welfare Department.

The Subcommittee on Planning consists of the Executive Committee members plus the institutional representatives. The Subcommittee on Utilization and Review consists of all the practicing physicians plus Dr. Patterson.

The Subcommittee on Utilization and Review receives claims under question at least monthly from Connecticut General, fiscal advisor to the State Welfare Department, and settles as many as it possibly can.

Claims referred to the Subcommittee for study and recommendation are those in which Connecticut General believes that the physician's "usual" charge is greater than the "customary" charge level prevailing in his area of practice. Questions of proper utilization also come under the Subcommittee's scrutiny, even though the charge itself may not be questioned.

Where circumstances warrant such action, cases are referred to the appropriate component county medical association for opinion. When that occurs certain procedures established by the Medical Advisory Committee are expected to be followed. The procedures have been thoroughly explained to chairmen of County Review Committees by Dr. Polivy and Dr. Hess, and the chairmen in turn have briefed their committee members. The steps are as follows:

1. The County Review Committee will discuss the case with the physician. (He will have been notified by Dr. Hess that the claim under question has been sent to the committee).

2. A reply to the Medical Advisory Committee is expected within 30 days; in difficult cases this period is extended to 90 days.

3. No payment of the disputed claim may be made until a decision has been rendered.

4. Once a claim is under study the physician concerned may not seek to negotiate a settlement with the State Welfare Department.

5. If a county review committee finds evidence of violation of medical ethics, its report and recommendation are forwarded to the Medical Advisory Committee and, in turn, the county medical association will be advised as to the disposition of the case by the Commissioner.

6. Policies established by the Medical Advisory Committee as working guides are published by the State Welfare Department in a periodic memorandum. Dr. Hess has already sent each physician a Bulletin for Physicians, in loose leaf form, containing information about program policies and procedures. Additional information sheets are sent to the physicians from time to time to update their knowedge of Medicaid.

Some of the policies are:

1. No artificial price increase (for example, injection as a chargeable item) will be accepted.

2. No charge for laboratory procedure done by the State Health Department will be accepted for payment.

3. A routine office visit will include a urine and hemoglobin test.

Now, what is being done for the physician? First, the Medical Advisory Committee believes he too should have an advocate. Each component county medical association has been asked to establish a committee, either a new one or a standing committee assigned the task, to receive complaints or handle problems raised by the practicing physician concerning any aspect of the program. This committee is then expected to discuss the matter with the Medical Advisory Committee and Dr. Hess.

Further, the Medical Advisory Committee maintains liaison with the Society's Council. This two-way exchange of information promotes a better understanding of the program and focuses on recurring problems which both are seeking to eliminate.

There is a Right to Know law in Connecticut and the news media will be reporting on the Title XIX program periodically. Physicians participating in the program should be aware of this fact so that printed accounts will reflect credit on the medical profession's conduct, purpose and cooperation.

The Subcommittee on Planning has an interesting assignment. Looking ahead, it attempts to devise ways of expanding the program through pilot projects, emphasizing preventive medicine and a more effective delivery of comprehensive health services on an ambulatory basis, always keeping in mind that beneficiaries are entitled to free choice of physician. Such approaches will help to reduce the crisis aspect of the health care received by welfare patients.

In summary, the Medical Advisory Committee is attempting to smooth out any wrinkles in the program during the one-year trial period ending March 1, 1969, when the "usual and customary" method of paying physician's charges will be evaluated and reported on to the General Assembly.

In the meantime, two conclusions can be drawn about Connecticut's Title XIX Program of Medical Assistance: physicians have supported the program and it has advanced the delivery of quality care to Title XIX beneficiaries.

More than 1,800 physicians are now participating in the Medicaid program, nearly 50 per cent of the practicing physicians in Connecticut. Formerly less than 400 participated in the welfare medical program.

Quality medical care for all people continues to be a goal of the Connecticut State Medical Society. A successful Medicaid program, supported by an increasing number of physicians, will help to reach the formerly hard to reach.

Nursing Action Toward Excellence

Ira Hiscock, M.P.H., Sc.D.

A Review

The tenth anniversary of the Regional Educational Program for Professional Nurses is a noteworthy milestone. Evidences of how nurses can influence the future of health care, responding constructively to increasingly expressed desires for excellence in patient care, are being appraised in the light of continuing change, cooperative planning, and exploration of interrelationships in various parts of our social structure. The first meeting on September 26 of the 1968 series of state-wide sessions, coordinated by the Connecticut League for Nursing, marked the continuing step in a plan first envisioned in 1954 and finally achieved in 1958.

For the initial exploration of the need for and wisdom of planning a cooperative approach in structuring continuing educational meetings for nurses, to be offered on a regional basis, representatives of some 22 official and voluntary health agencies were invited to meet. There was discussion of ways and means through which much duplication of effort, planning and financing, might be minimized and coordinated planning achieved. In the words of one of the leaders in this venture, Alba A. Mastorgi, R.N., B.S., "Testimony to the fact that successful regionalization can be achieved is evidenced by the consistently increasing attendance by our nurses at these meetings and the sustained interests and support of all the original participating agencies.—A dedicated group, plus a plan based on expressed needs, plus interpretation, plus coordination equals enthusiastic, sustained interest and participation." This is said to be the formula consistently subscribed to by the many nursing and allied health leaders who have served so ably on the various committees.[1]

The keynote address in the morning session of this year's series was so comprehensive and timely that a brief review is given below. This was followed by description of the Connecticut Regional Medical Program: Its Progress and Plans, by Henry T. Clark, Jr., M.D., Program Coodinator, and Mrs. Elsa L. Brown, R.N., M.Ed., member of one of the 9 task forces. The opening address was given to a "packed house" in a double room of the Stratford Motor Inn, who enthusiastically requested copies for further study. Their wish is being met by publication of the morning's proceedings and distribution by the Connecticut League for Nursing.

Miss Edith V. Olson, R.N., M.S., the speaker, is nursing coordinator of the Rochester, N.Y., medical program for heart disease, cancer, and stroke, of the University of Rochester Medical Center. She knows the Connecticut scene, having worked here for a few years on the staff of the Yale School of Public Health. She defined Regionalization as the organization and coordination of all of the health resources and services within a defined area, for the purpose of maintaining the highest possible level of medical care, and of adapting a comprehensive health program to the characteristics and needs of the area. That regionalization has become a contemporary social phenomenon, the urge to hold costs down, the increasing desire for standards of excellence, and some barriers, were noted; besides references to the "doctrine of state primacy," and to links of hospitals and university centers, coupled with the importance of communication and understanding on the part of all concerned.

Characteristics of regionalization include enabling delivery of scientific advances to health service level; functional mechanism for linking research, manpower, finances, and facilities to health service level; geographic features; recognition and utilization of individual strengths and resources; coordination; continuous process. This process of regionalization calls for involvement; for identifica-

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[1] The 1968 program cover, on the theme of Challenges for Nursing Action, shows coordination by the Connecticut League for Nursing, sponsored by: American Cancer Society, Connecticut Division; Connecticut Heart Association; Connecticut Nurses Association; Connecticut State Department of Health Connecticut Tuberculosis and Health Association; Easter Seal Society for Crippled Children and Adults of Connecticut; with contributions also from Connecticut Association for Mental Health, The Connecticut Association for Extended Care Facilities, The Connecticut Hospital Association, and The Board Members Organization of Connecticut Public Health Nursing Agencies.

IRA HISCOCK, Emeritus Professor Public Health, Yale University, Member of the Connecticut Welfare Advisory Citizens Board and of the Public Health Council.

tion of needs and opportunities; for assessment of resources; for clear definition of objectives; for setting of priorities; for proper implementation; and for periodic evaluation of plans, measures, and results.

The real challenge for nursing participation (and likewise for another professional and even co-professional people concerned) has numerous aspects, including: being informed; being willing to experiment; becoming skilled in interpersonal relationships; becoming involved; being cooperative; utilizing community leadership; being in pursuit of excellence, and being involved in change, with judgement to know when and if change is necessary.

Some five decades ago, Mr. Elihu Root wrote, in expressing his conception of an experiment in world order, as follows:

"The real power behind international as well as national progress toward better conditions is public opinion. Public opinion, however, cannot make itself affirmatively effective except by the creation of institutions adapted to give it effect. Mere verbal expressions of opinion get nowhere . . . What is everybody's business is nobody's business. To get things done some human agency must be designated to give effect to the general desire that they be done."[2]

During the past ten years, the Connecticut League for Nursing has been a potent force in helping to "get things done" that benefit not only professional nurses, but also many others who have become involved in health care of people.

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[2] Pioneers in World Order, edited by Harriet Eager Davis, Columbia University Press, New York, 1944, with Foreword by Raymond B. Fosdick, page V.

Appreciation Of Physical Signs

Is is sometimes suggested that learning to appreciate many signs, particularly those arising from the chest, is very difficult. The beginner, it is said, when examining with the greatest care a case of early pulmonary tuberculosis, may detect nothing wrong. Whereas the expert, with the aid of his trained senses of hearing and vision, may be able to find an occasional rale, a slightly prolonged expiratory sound, minor variations in the percussion note, almost imperceptible flattening of one part of the chest, and slight impairment of movement of one side. But such inconspicuous signs are hardly significant. Variations between the chest appearances of normal people, or in the same individual between different parts of the chest, are surely as great as are those presented by many of these signs. They do not justify the diagnosis of pulmonary tuberculosis if the radiograph is normal in every view and the sputum is free of tubercle bacilli; and if there is real evidence of the disease they should not influence the opinion of the state of the chest. Similar criticism can be made of other inconspicuous signs, such as slight pallor of an optic disc, an equivocal plantar response on both sides, a "slapping" first heart sound, or an increased area of splenic dullness on percussion. If there are other reasons for coming to a diagnosis their aid is not required; if they are alone they justify no diagnosis. Trivial deviations from the average can be discovered in any man if they are looked for hard enough.

The appreciation of physical signs is, then, not the difficult matter it is sometimes held to be. The signs of real value are those which are striking, and which anyone, *provided he seeks for them,* can appreciate.—Todd, J. W.: The Superior Clinical Acumen of Old Physicians: A Myth, *Lancet,* 1:482 (March 7) 1953.

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The trial period is brief: 1 week. Try one tablet q.i.d. at first. Tandearil usually starts working within 3 to 4 days. When response occurs, as little as 1 or 2 tablets daily may hold back pain and stiffness, and increase joint motion.

On the next page is a summary of adverse reactions, contraindications, warning and precautions.

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For brief summary see next page.

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Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.

Warning: This drug is an analog of phenylbutazone; sensitive patients may be cross-reactive. If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Persistent or severe dyspepsia may indicate peptic ulcer; perform upper gastrointestinal x-ray diagnostic tests if drug is continued. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with caution in the first trimester of pregnancy, and in patients with thyroid disease.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patients should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia), sudden weight gain (water retention), skin reactions, black or tarry stools or other evidence of intestinal hemorrhage occur. Make complete blood counts at weekly intervals during early therapy and at 2-week intervals thereafter. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The more common are nausea and edema. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension, the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately after meals or with milk to minimize gastric upset. Drug rash occasionally occurs. If it does, promptly discontinue the drug. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), or a generalized allergic reaction similar to a serum sickness syndrome may occur and require permanent withdrawal of medication. Agranulocytosis can occur suddenly in spite of regular, repeated normal white counts. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, hypersensitivity angiitis, pericarditis and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

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Initial: 3 to 6 tablets daily in divided doses. Usually unnecessary to exceed 4 tablets daily. A trial period of one week is considered adequate to determine the therapeutic effect of the drug. Maintenance: Effective level often achieved with 1 or 2 tablets daily, should not exceed 4 tablets daily.

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REGIONAL WORKSHOPS — 1968-69

The Eastern Region, of which Connecticut is a part, is composed of the six New England states, New York, New Jersey, Pennsylvania, Delaware, Maryland, Virginia, West Virginia, and the District of Columbia. On October 17 and 18 representatives from all these states joined in a Regional Workshop at the Statler Hilton in Boston. Each state was permitted to send the following state chairmen: AMA-ERF, Health Careers, Safety-Disaster Preparedness, Community Health, Mental Health, and Presidents-elect. Since the AMA underwrites some of the expenses incurred in holding a workshop, the men should be somewhat interested in the purposes and quality of the programs. One purpose is to create a closer bond between national and the states; the other to inform the states of programs available and to train women in their participation of these programs. It has been emphasized this year especially that a state or county is not under obligation to undertake every program which national offers, but the choice available should be known to be used effectively by state or county.

The AMA-ERF currently sponsors six programs with the auxiliary pledging its financial support to the Institute for Biomedical Research and funds for medical schools. Although the auxiliary is not actively seeking funds for the Loan Guarantee Fund this year, contributions are being accepted and credit will be received. Last year AMA Woman's Auxiliary contributions to AMA-ERF totalled $388,681.84.

The purpose of the Health Careers programs is obviously to interest more people in working in the health field. It has been forecast that within a few years one out of every seven high school graduates will be needed in health work. "Health Career Opportunities and Training Programs" charts have now been compiled by state and region. Though there are constant changes, the charts give a picture of what health training programs we have, what we need, and the wide gap between what we have and what we need. There is also a great need for refresher courses to return the inactive trained health worker to a job. The medical profession and its auxiliary must accept the responsibilities involved in education and preparation of health field workers in all categories.

The Safety-Disaster Preparedness Committees are interested in school pedestrian safety, poison control GEMS (Good Emergency Mother Substitute) in the safety category. This Block Mother Plan involving safe havens for children ½ hour before and ½ hour after school in case of emergency or disaster, and training programs for ambulance personnel come under the Disaster Preparedness label.

The possible programs available under the heading of Community Health are the most numerous of any committee. A few are blood donor recruitment, emergency medical alert indentification tags for children, health fairs, immunization programs, and package programs on narcotic addiction and venereal disease.

Dilemmas of the adolescent and young adult involving the use and abuse of alcohol are studied by the Mental Health committees. Guidance toward the proper use of alcohol by use of the package program "The Use and Not Abuse of Alcohol" can be carried out. Interest is also shown in the mental health of children, suicide prevention and help for the mentally retarded.

The part of the Regional Workshop involving the presidents-elect was concerned particularly with auxiliary program development and auxiliary membership with the hope of increasing it to a closer ratio with the Medical Society.

In Memoriam

Brown, Virginia H.—Niantic, Ohio State College of Medicine, 1948. Dr. Brown was a general practitioner in the Niantic area for over ten years. She was associated with the Lawrence and Memorial Hospital. She was a member of the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Brown died July 29, at the age of 48.

Connor, Joseph J.—Hartford, Yale University School of Medicine, 1930. Dr. Connor was a specialist in ophthalmology in Hartford for over 30 years. He was associated with St. Francis Hospital. He was a member of the Hartford City Medical Society, the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was a Diplomate of the American Board of Ophthalmology and a Fellow of the American Academy of Ophthalmology and Otorhinolaryngolgy. Dr. Connor died October 16, at the age of 64.

Dickenson, James R.—East Norwalk, Pittsburgh University School of Medicine, 1944. Dr. Dickenson was a practicing psychiatrist and director of the Norwalk Hospital Psychiatric Clinic. During World War II, he was commissioned as a captain in the U.S. Army Medical Corps and served as chief surgeon aboard the Queen Mary from 1943 to 1946. Dr. Dickenson had practiced at the Silver Hill Foundation and had been connected with the Mental Hygiene Clinic in New York City. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Dickenson died October 14, at the age of 50.

Eisenberg, Henry—Hartford, University of Berlin, 1930. Dr. Eisenberg was chief of the State Health Department's Chronic Disease Control Section. During World War II he was a colonel in the Army. He had been director of the Cancer Registry, past president of the Connecticut Health League, member of the executive board of the Cancer Society, and past member of the executive board of the Heart Association. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the International Cancer Association. He was a consultant to the World Health Organization, the Hartford Hospital, and Mount Sinai Hospital. Dr. Eisenberg was on the teaching staff at Yale University School of Medicine. In 1967, he was a recipient of the National Cancer Society medal for distinguished service in cancer control. Dr. Eisenberg died November 2, at the age of 63.

Placement Opportunities

PEDIATRICIAN for a rapidly growing community in Western Connecticut. Present pedatrician wants to concentrate solely on subspecialty. Arrangements on solo, salary or associate basis.

EMPLOYEES' PHYSICIAN—physician for employees' clinic, whose duties would consist of preemployment and annual physical examinations, daily sick call, and occasionally immunizations, hours from 8:00 a.m. to 5:00 p.m. with an hour for lunch, Monday through Friday. Four weeks' vacation after one year and excellent fringe benefits. Salary of $20,000 per annum.

PEDIATRICIAN—Three member partnership in Obstetrics and Gynecology is looking for a pediatrician for the Enfield, Connecticut area which serves a population of 60,000. An office is immediately available in a new air-conditioned Medical Building.

WANTED: PSYCHIATRIST—Opportunities exist in State Welfare Department for (1) a Psychiatrist to administer and coordinate the Mental Health Program; (2) Psychiatrists to act as District Welfare Department Consultants for the Mental Health Care Program. Contact: Orvan W. Hess, M.D., Medical Director, State Welfare Department, 1000 Asylum Avenue, Hartford, Connecticut 06115.

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Welcome, New Members

Fairfield County

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Burton I. Benjamin, M.D., 19 Third Street, Stamford, Conn. 06902.

Peter E. Bogdan, M.D., 49 Lake Avenue, Greenwich, Conn. 06830.

Irwin Broudy, M.D., 881 Lafayette Street, Bridgeport, Conn. 06603.

Paul V. DiGrazia, M.D., Route 7, Brookfield, Conn. 06804.

Edwin H. Dombrowski, M.D., 95 Morgan Street, Stamford, Conn. 06905.

Andrew C. Fazzone, M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.

William J. Gacso, M.D., 2820 Main Street, Bridgeport, Conn. 06606.

George A. Garofalo, M.D., 30 D'Eramo Place, Bridgeport, Conn. 06606.

Philip M. Gaynes, M.D., 1700 Post Road, Fairfield, Conn. 06430.

Edwin Hankin, M.D., 1700 Post Road, Fairfield, Conn. 06430.

Jens H. Hermann, M.D., 166 East Avenue, Norwalk, Conn. 06851.

Donald R. Homer, M.D., Danbury Hospital, Danbury, Conn. 06810.

Enrique Izurieta, M.D., 881 Lafayette Street, Bridgeport, Conn. 06603.

Martin J. Krauthamer, M.D., 10 Corbin Drive, Darien, Conn. 06820.

Paul K. Maloney, Jr., M.D., 12 Elmcrest Terrace, Norwalk, Conn. 06850.

Sergio G. Manimbo, M.D., 750 Summer Street, Stamford, Conn. 06902.

Karl H. Mueller, M.D., Silver Hill Foundation, New Canaan, Conn. 06840.

Harold T. Oesau, Jr., M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.

Lewis M. Portnoy, M.D., 695 Park Avenue, Bridgeport, Conn. 06604.

Neil C. Raff, M.D., 6 Village Square Westport, Conn. 06880.

Silvio A. Salerno, M.D., Greenwich Hospital, Greenwich, Conn. 06830.

Stanley Saperstein, M.D., 43 South Main Street, Newtown, Conn. 06470.

John A. Simpson, M.D., 1026 Park Avenue, Bridgeport, Conn. 06604.

Bernard Singer, M.D., 104 East Avenue, Norwalk, Conn. 06851.

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Louis M. DeNegre, M.D., 2044 Bridgeport Avenue, Milford, Conn. 06460

John V. Federico, M.D., 789 Howard Avenue, New Haven, Conn. 06504

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John A. Godley, M.D., 111 Park Street, New Haven, Conn. 06511

Felix I. Gottlieb, M.D., 1484 Chapel Street, New Haven, Conn. 06511

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Jerold J. Principato, M.D., 789 Howard Avenue, New Haven, Conn. 06504

Leonard R. Prosnitz, M.D., 789 Howard Avenue, New Haven, Conn. 06504

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Irving Shiffman, M.D., 219 West Main Street, Meriden, Conn. 06450

Stanley D. Stier, M.D., 435 New Haven Avenue, Derby, Conn. 06418

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Sheldon G. Gilgore, M.D., Eastern Point Road, Groton, Conn. 06340.

Milton Harrison, M.D., Boston Post Road, Old Lyme, Conn. 06371.

Alexander Parthenis, M.D., Box 508, Norwich, Conn. 06360.

Charles H. Robinson, Jr., M.D., 276 Montauk Avenue, New London, Conn. 06320.

Morton Solomon, M.D., Chas. Pfizer & Co., Inc., Medical Research Labs., Groton, Conn. 06343.

Litchfield County

Richard N. Collins, M.D., Sharon Clinic, Sharon, Conn. 06069.

Henry Fearon, M.D., Washington Green, Washington, Conn. 06793.

Beverly C. Pass, M.D., 71 Spencer Street, Winsted, Conn. 06098.

John M. Pierce, M.D., 71 Spencer Street, Winsted, Conn. 06089.

Joseph P. Tumblety, M.D., Indian Mountain Road, Lakeville, Conn. 06039.

Placement Wanted

INTERNIST—subspecialty in Infections Diseases, recently completed residency, desires association or group practice.

NEUROLOGIST & PSYCHIATRIST—Board certified in both specialties, desires association with individual or group in Eastern Connecticut.

OBS-GYN—Board eligible, military obligations completed, wishes associate practice starting July, 1969. 30 years of age, married, and has National Boards.

G.P.—Physician, age 30, military obligations completed, desires general practice or emergency room slot in Connecticut. Available immediately. Has Connecticut license and National Boards.

SURGEON—38, Board certified, Connecticut license. Presently in service, wishing to terminate active duty because of increasing administrative work and wishes to be in direct patient care. Available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Electrocardiography: A Programmed Text. Edited by S. G. Owen, M.D. Little, Brown and Company, Boston, 1967. 180 pp. Illustrated.

Synopsis Of Surgery. Edited by Richard D. Liechty, M.D. and Robert T. Soper, M.D. The C. V. Mosby Company, Saint Louis, 1968. 1091 pp. With 346 illustrations. $12.50.

Atlas Of Precautionary Measures In General Surgery. Edited by Ivan D. Baronofsky, M.D., Ph.D. The C. V. Mosby Company, Saint Louis, 1968. 281 pp. Illustrated with 111 plates and 132 figures. $23.50.

Cystic Fibrosis. Ciba Foundation Study Group No. 32. Edited by Ruth Porter and Maeve O'Connor. Little, Brown and Company, Boston, 1968. 150 pp. 8 illustrations. $3.95.

Hearing Mechanisms In Vertebrates. A Ciba Foundation Symposium. Edited by A. V. S. de Reuck and Julie Knight. Little, Brown and Company, Boston, 1968. 324 pp. 107 illustrations. $12.00.

The Mentally Abnormal Offender. A Ciba Foundation Symposium. Edited by A. V. S. de Reuck and Ruth Porter. Little, Brown and Company, Boston, 1968. 260 pp. 2 illustrations. $10.00.

Electrocardiography and Vectocardiography. Fourth Edition. Edited by E. Grey Dimond, M.D. Little, Brown and Company, Boston. 152 pp. 179 illustrations. $7.50.

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LABORATORY MEDICINE

"Unsolicited" Laboratory Information

It is currently popular to perform many laboratory tests on a routine basis without clinical indication. These tests can be done inexpensively and fairly reliably on a mass scale. An interesting study by Young and Drake (Technicon Symposium 1965) attempts to evaluate the usefulness of this data.

398 patient "profiles" including blood glucose, BUN, creatinine, Na, K, Cl, CO_2, Ca, phosphorus, Alk. p'tase, bilirubin, SGOT, PBI, cholesterol, Hg, ESR, blood smear and routine urinalysis were performed although not ordered. These data were not furnished the attending physicians until after the patients were worked up as indicated and were under appropriate treatment. With the new information the cases were then discussed and changes in diagnosis or treatment made as decided.

I analyzed their data and created 4 categories—Helpful (Yes or No), and Hindrance (Yes or No) based on whether the extra tests added to the diagnosis or treatment in a fashion which benefitted the patient. A lab error or unexplained value which caused the patient to receive further fruitless studies was considered a hindrance.

Helpful —	Yes —	10
	No —	388
Hindrance —	Yes —	85
	No —	313

Apparently this type of "profile" is over 8 times as likely to be a hindrance as a help in patient care!

Dangerous Sodium Levels

Low—below 115 serious, below 110 threaten life, below 105 damage brain.

Usual Cause—water intoxication due to giving water without salt. Low sodium can be prevented by 500 ml daily of normal saline plus replacement of excess loss.

High—above 170, damage brain.

Common cause—oral tube feeding with inadequate water in comatose patients.

Rapid change in either direction is dangerous.

Surgery and Water

"Nothing PO" from night before surgery leads to dehydration by the time of surgery. Use of 500-700 ml per hour of lactate–Ringers during surgery combats fluid loss, prevents shock, prevents renal damage. One-half of blood loss can be replaced by 2-3 times as much lactate-Ringers.

(Adapted from Gambino, 1968)

Clinical Pathology Residents

In our 4 year approved Residency the 3rd and 4th year Residents are assigned to Clinical Pathology and are always available for consultation and assistance. They can take care of many questions and problems if you need special tests or can't get a laboratory problem straightened out, particularly nights and weekends. Ask the telephone Operator to get you the Resident in Clinical Pathology.

Coproantibodies

Coproantibodies are antibodies present in intestinal fluid or in feces. These antibodies behave independently of serum antibodies. They are produced by the small bowel. Herskovic[1] in his work "Gluten Intolerance Following Cow's Milk Sensitivity" concludes that the presence of coproantibodies to milk protein and to fraction III of gluten is a rapid and probably specific means of diagnosing milk or wheat sensitivity.

Using gel-diffusion techniques and 12 different antigens (whole milk, skim milk, gluten, wheat, soy, rye, oat, egg albumin, bovine albumin, lactoalbumin, Lactobacillin and Veilonella) we are doing antibody determinations in stool and serum and studying their relationship with the principal fractions of gamma globulin (A, M, G).

With these tests we hope to assist in the diagnosis of food allergies, other allergic disease, chronic inflammatory disease of the bowel, and irritable bowel syndrome.

Signed: R. Enriquez, M.D.

Intracaths Abandoned

After several unpleasant accidents we have removed all Intracaths from the hospital.

Roy N. Barnett, M.D.

DOCTOR—Does your wife like to read the Auxiliary news? Then be sure and take your copy home.

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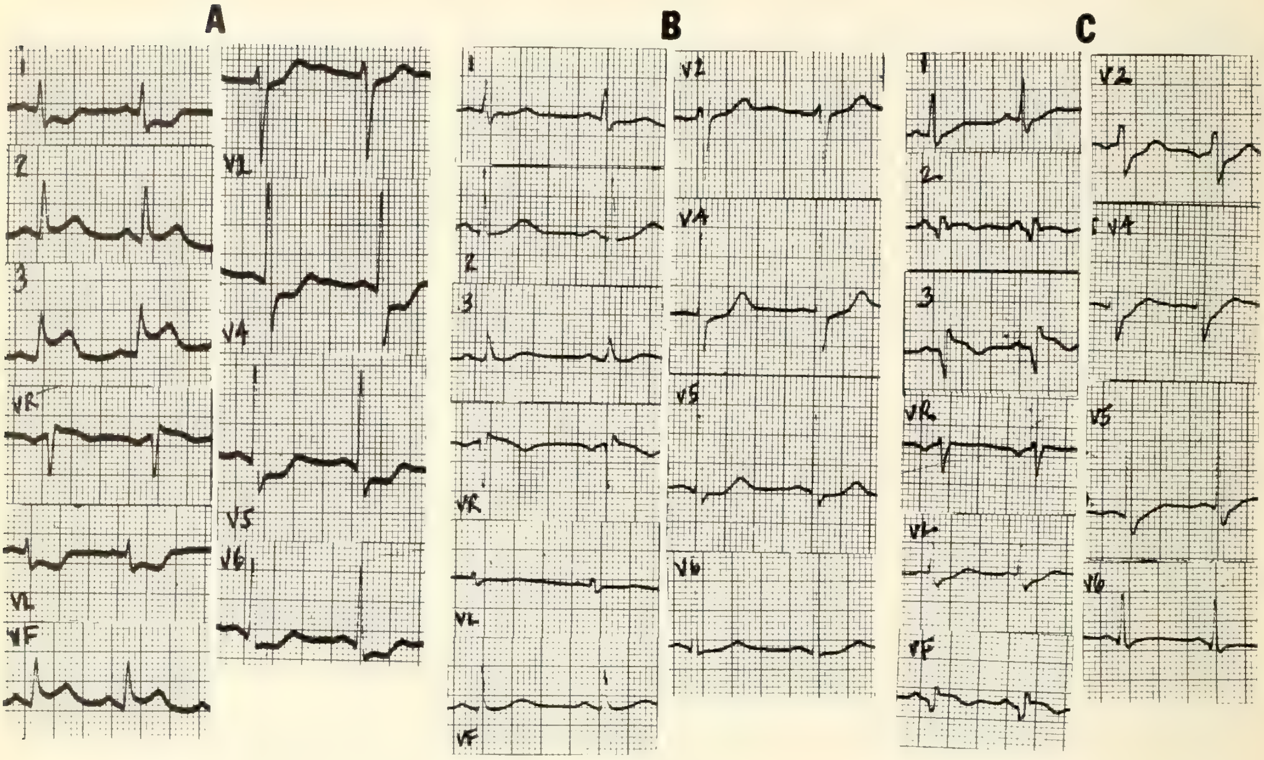
[1] Annals of Allergy, *26*, 33, Jan. 1968.

Electrocardiograms of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Director—Department of Electrocardiography
Memorial Unit



6-16-67
12 NOON

6-16-67
2 P.M.

7-6-67
2 P.M.

Tracing A was taken shortly after admission of a 56 year old white male while the patient was still having severe pain of sudden onset while at rest. He gave a history of angina of effort and nocturnal angina.

Tracing B was taken about two hours later when the pain had completely subsided. Repeat tracings daily for the next six days revealed no significant changes in the QRST patterns. Serial enzyme studies, sedimentation rates and leuocoyte counts were normal. No fever developed. The patient remained symptom free and was discharged after ten days.

Tracing C was taken three weeks later after another bout of severe substernal pain, requiring hospitalization.

Which of the following is the most likely diagnosis at the first admission on June 16, 1967?

1. Acute Pericarditis
2. Pulmonary Embolism
3. Acute Inferior Wall Infarction
4. Variant form of Angina Pectoris

Discussion

In the classic type of angina pectoris, pain occurs when the heart work is increased and is relieved by rest or the use of nitroglycerine. The electrocardiogram taken during pain usually exhibits depression of the ST segments without reciprocal elevation. In the variant form of angina pectoris, first fully described by Prinzmetal et al the pain usually occurs at rest or during ordinary activity or during sleep, and may not occur with exercise. The pain may be protracted and recur in cyclic fashion. During such an attack the electrocardiogram reveals reciprocal ST segment changes, of the type usually seen in the presence of acute infarction. These changes are transient and subside when the chest pain is gone. No abnormal Q waves develop. The variant form of angina may continue for years without infarction, but when infarction does occur its location corresponds to the area of myocardium which gives rise to the ST elevation seen during the attack of angina.

Tracing A taken at 12 noon on June 16, 1967 reveals elevation of the ST segments in leads 2, 3, VR and VF, and depression of the ST segments in leads 1, VL, V2-V6. No abnormal Q waves are noted. These patterns are consistent with acute injury current arising in the inferior wall.

Tracing B taken at 2:00 P.M. on June 16, 1967 reveals ST segments within normal limits except for minimal junctional type ST sepression in V4-V6.

Tracing C taken at 2:00 P.M. on July 6, 1967 reveals abnormal Q-waves in leads 2, 3 and VF, and reciprocal ST segment changes characteristic of recent infarction of the inferior wall. Serial enzyme studies confirmed the diagnosis of a recent infarction.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

Louis H. Nahum, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

NEWS BRIEFS

Changes in Medicine

Dwight L. Wilbur, M.D., President of the AMA, predicts that the practice of medicine will change drastically in the next 10 to 15 years. He says:

. . . of the family physician. "The family doctor will be almost as extinct as a dodo. When you're hurt or sick, you'll go to the nearest hospital for emergency treatment, administered by a physician especially trained in these procedures. The kindly old gentleman with the bedside manner was wonderful in his day, but society can no longer afford him. The modern doctor is more efficient, more scientific and less subject to error."

. . . of group practice. "Group practice is the growing trend. It saves the doctor's time—there aren't nearly enough of them to go around—and it saves the patient's money." Patients seen in the emergency room may be "referred to a specialist, working not in a private office but in a large center with other specialists, sharing facilities they singly could not afford. You may not be seen by the doctor on your initial visit. Your case history will be taken by assistants—even, eventually, by computers. Trained aides may do some of the preliminary examination."

. . . of barriers to medical care. "One is ignorance of the benefits which we find in many slums and rural areas. Some simply do not know what modern medicine can do for them and they turn to self-medication or to quacks. Two closely linked barriers are financial and geographical. Even where the medical service is free, it may cost a sick person all of a working day to go to and from a distant medical center. Then there's the status barrier. Minority groups are not comfortable in the presence of doctors. They find it difficult to communicate with educated personnel."

ER Service

Five physicians on full-time salary will run the St. Francis Hospital (Hartford) emergency room on a round-the-clock basis, according to a report in the Hartford Courant. The shift to a full-time emergency room staff follows a national trend. New Britain General converted to the same system recently. It means that these doctors give up office practice and become "specialists" in providing quick diagnosis and as much treatment as their training permits. Staff interns and residents will also be available.

New Medical Practitioner

A new kind of medical practitioner will be trained at the University of Colorado Medical School in an attempt to meet what is termed "an impending crisis in health care for children." The workers (they may be called child care associates) will meet the medical needs of children who don't require special attention or care for serious ailments. The training will include two years of undergraduate study, two years at the medical school in basic sciences and clinical experience, and a one-year internship. Bachelor's degrees are awarded to those completing the course.

Norwalk Child Care Center Opened

A group of Norwalk area pediatricians have opened a children's medical center in a converted garage in that city. Its objective is to provide optimum professional care for youngsters from infancy to 16 years at a price their parents can afford to pay. Fees will be based on parent incomes. Eleven physicians are volunteering their services to staff the clinic during office hours and to respond to calls for medical assistance at other times. Another objective of the center is continuity of medical care with the same physician treating a particular child at each visit. The physicians will be at the center, on a rotating basis, from 6:00 P.M. to 9:00 P.M. Monday through Friday, and from noon to 3:00 P.M. on Saturday.

Higher Medicaid Limits

State Sen. Gloria Schaffer has indicated she would like to see Connecticut fill the "income gap" in the current medicaid program. She told the audience at a recent public hearing that "the maximum income for persons eligible or medicaid assistance—$2,500 a year for a couple—is ridiculously low." She would like to see the maximum raised to around $8,000 a year for a family of four.

Mount Sinai Expansion

Construction work has begun on a $13.5 million building expansion of Mount Sinai Hospital, Hartford. A new nine-level west building and a five-level addition to the east wing will provide space for up to 217 new beds, two teaching classrooms, a 150-seat multi-purpose auditorium, enlarged intensive care unit and coronary care unit, enlarged operating room and recovery room, and new cystoscopic, orthopedic and neurosurgical rooms.

MEETINGS

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospital's Auditorium, New London

January 4 **7:15 P.M.**

Biochemical and Physiological Approach to Pancreatitis

Philip J. Snodgrass, M.D., Chief, G. I. Division, Peter Bent Brigham Hospital; Associate in Medicine, Harvard Medical School.

January 28 **7:15 P.M.**

Nitrogen Intoxication in Liver Diseases, Its Causes and Treatment

C. Thomas Nuzum, M.D., Research Fellow in Medicine, Peter Bent Brigham Hospital

CANCER

Oncology

Russ Home Conference Room, Griffin Hospital, Derby

Sponsored by the Connecticut Division of the American Cancer Society and the Yale School of Medicine

January 14 **8:00 A.M.-9:00 A.M.**

Management of Head and Neck Cancer

Speaker: Joseph Cleveland, M.D., Instructor in Surgery, Yale School of Medicine

February 4 **8:00 A.M.-9:00 A.M.**

Radiotherapy in Initial Tumor Management

Speaker: Carl vonEssen, M.D., Associate Professor of Radiology, Yale School of Medicine

February 11 **8:00 A.M.-9:00 A.M.**

Radiotherapy in Control of Metastatic Disease

Speaker: John Mallams, M.D., Visiting Professor of Radiology, Yale School of Medicine

Chairman: Ronald DeConti, M.D., Yale School of Medicine

Co-ordinator: Vincent A. DeLuca, Jr., M.D., Derby

Open to all physicians.

MEDICINE

Wednesday **12:00-1:15 P.M.**

Medicial Chest Seminar

Radiation Center Conference Room, Hospital of St. Raphael, New Haven

Sponsored by the Section of Chest Disease, Department of Medicine, Hospital of St. Raphael

Chairman: John B. Berte, M.D., Director, Department of Pulmonary Disease and Inhalation Therapy, Hospital of St. Raphael

Open to all physicians

Thursdays **1:30 P.M.-3:30 P.M.**

Clinical and Laboratory Hematology

Hematology Laboratory and Wards, Hospital of St. Raphael, New Haven

Sponsored by Hematology Service, Department of Medicine, Hospital of St. Raphael

Chairman: Robert P. Zanes, Jr., M.D., Hospital of St. Raphael

PEDIATRICS

December 11 **2:00 P.M.-4:30 P.M.**

Solid Tumors of Childhood

Anatomy Lecture Room (204), Yale University Sterling Hall of Medicine, New Haven

Sponsored by Yale University School of Medicine

Speakers: Lawrence K. Pickett, M.D., Professor of Surgery and Pediatrics; Howard A. Pearson, Professor of Pediatrics; Joseph H. Galicich, M.D., Assistant Professor of Heurosurgery.

Fee: $5.00; limited to first 100 registrants; fee waived for interns and residents

PSYCHIATRY

Seminars sponsored by the Connecticut Valley Hospital, held in Merritt Hall Auditorium

January 14 **10:30 A.M.**

Group Psychotherapy and Group Process, Maurice E. Linden, M.D.

January 21 **10:30 A.M.**

Industry, Politics and Psychiatry, Bernard L. Pacella, M.D.

SURGERY

January 9

Third Annual Meeting of the Connecticut Chapter of the American College of Surgeons

Hotel America, Hartford

"Quality Surgical Care—A Challenge from Modern Society." Panel discussants will include providers of surgical care, a hospital administrator, and a third party payee representative.

Contact: Francis Coughlin, M.D., Secretary-Treasurer, Connecticut Chapter, American College of Surgeons, 144 Morgan Street, Stamford.

BOOK REVIEWS

CURRENT THERAPY 1968. Edited by Howard F. Conn, M.D. W. B. Saunders Company, Philadelphia, 1968. 898 pp. $14.00. Canadian price: $15.15.

Reviewed by: LOUIS H. NAHUM

This book contains the latest approved methods of treatment for the practicing physician. It begins with two extremely valuable pages of normal laboratory values and ends with two such pages of extreme clinical importance. At the end is a chapter on acute poisonings. It also lists the poison control centers in the whole country listing nine in Connecticut. There are given poisonous substances in common household items. There is an index of twenty-seven pages and also metric and system apothecary. There is a table of weight for men and women. In short with this one volume a physician can be knowledgeable on the latest methods of treating any disease.

This volume is the 20th of a series of annual publications. The first edition was published in 1949 at the dawn one might say of one of the most productive and unprecedented eras in the history of medical therapeutics. Penicillin was just coming in and its dosage not well established, many diseases were just beginning to come under control and the great advances in immunization against the common serious childhood diseases were yet to come. Cortisone and ACTH were not mentioned. B_{12} in pernicious anemia was only suspected.

We are now at the beginning of an era in which specific agents in the treatment of virus diseases may be utilized. Two such drugs idoxuridine (IDU) and amandatine may be the first of this era and are included in this edition. Somehow the use of long acting nitrates in relation to formation of methemoglobin has escaped mention, although this fact requires a certain sophistication in the employment of these drugs.

As one reads through this volume it is difficult to escape the conviction that prudent and intelligent treatment of a patient requires that the physician have this indispensable book on his desk for daily reference. It is recommended for students, practicing physicians and specialists as a must.

CATECHOLAMINES IN CARDIOVASCULAR PHYSIOLOGY AND DISEASE. Ed. by Ralph Reader, D. Phil., New York: American Heart Association, Inc., New York, N. Y., 247 pages. $3.00.

Reviewed by: HERBERT LEVINE

This American Heart Association monograph consists of twenty-five papers presented at a conference held in Canberra, Australia, in January of 1967, and a brief but informative historical introduction by the editor. Two thirds of them are from Australian laboratories.

The first series of papers has to do with experimental investigations of the structure and function of the adrenergic nerve granules where catecholamine uptake, storage, and release take place. A second group deals with aspects of chemical and electrical transmission at various points along the sympathetic pathways. Sjoerdsma presents a brief review of his well-known work on the role of catecholamines in hypertension and drug therapy thereof. The remainder of the papers consider such subjects as the effect of catecholamines on platelet aggregation and blood kinin levels.

The last two papers deal with beta-adrenergic blockade and propanalol. Jose and Stitt, of Sydney, Australia, introduce the concept of the "intrinsic heart rate", which obtains after selective autonomic nervous system blockade with propanalol and atropine, and is reputed to resemble that of a classical "heart-lung" preparation. In heart disease this variable supposedly decreases in parallel with depression of contractile performance. The authors cite experiments with dogs whose cardiac performance is altered by drugs. This is an interesting attempt to separate some of the parameters involved in cardiac function. The second of this group of papers, by Bloomfield and Sawton of London, presents evidence to indicate that the depression of cardiac output produced by propanalol is independent of the effect on rate.

This monograph contains a great deal of information about contemporary research in this subject, although little of it is of immediate clinical usefulness.

CELL DIFFERENTIATION. A Ciba Foundation Symposium. Edited by A. V. S. DeReuck and Julie Knight. Little, Brown & Company, Boston, 1967. 256 pages with 43 illustrations.

Reviewed by: HOLLIS N. TRUAX

The contents of this book represent a symposium on cell differentiation held 31st January-2nd February 1967 in London. The membership at the meeting included twenty-four scientists from various parts of the world. The book contains fourteen papers and the general discussions following them. The papers cover selected topics and no attempt to cover the entire field of cell differentiation is intended.

Basically cell differentiation investigation focuses on the underlying mechanisms which make the primitive and developing cells react in certain predictable ways. Each speaker, naturally enough, presents an aspect of cell differentiation in which he is fluent. The titles of a few of the papers are: Possible mechanism of the Transfer of Information Between Small Groups of Cells; Cellular Synthetic Activities in Induction of Tissue Transformation; The Problem of the Chemical Nature of Embryonic Inducers.

It becomes obvious to the reader that the mysteries of cell differentiation are many and the hard facts are few. No ideal test animal exists and data gathered from different animals often conflicts. Progress, however, is being made but many answers will come only with the development of finer research tools. The membership at the meeting fully appreciate their degree of sophistication and the editors state in the preface:

"If more questions are raised than answered in this symposium, we feel that this may in itself be a fruitful contributor to progress in this vital field."

The symposium has little practical knowledge to offer to the average physician. Its main usefulness may be that it documents man's understanding of cell differentiation as of 1967.

ELECTROCARDIOGRAPHY: A Programmed Text For Self-Tuition In The Principles Of Electrocardiography And The Interpretation Of The Electrocardiogram. Edited by S. G. Owen, M.D. Little, Brown and Company, Boston, 1967. 180 pp. Illustrated. $9.00.

Reviewed by: LOUIS H. NAHUM

This book was originally written by Dr. Owen with the assistance of the Programme Division of International Tutor Machines. It is one of the first programmes of length to come out of a British University. It shows how material which is logical, self-contained and well adapted for visual presentation can be programmed. In particular it indicates the potential of this method of teaching, not merely in medical education, but at university levels generally.

Only a working knowledge of elementary anatomy, physiology and pathology is presupposed. In most cases the reader's own response to a multiple choice situation determines the reading sequence: the purpose of the question being to select the information which he, at that point, requires. In this way programme adapts to individual difficulties and the learning process proceeds at the learner's pace. When the reader has learned or understood the subject under current discussion, the programme then directs him to the next item in the logically developed main sequence of new information which constitutes the backbone of the book.

In addition to the multiple choice technique there is another: the occasional introduction of questions requiring constructed responses, especially when it seemed particularly appropriate to the learning situation. Like the multiple choice method, it demands the reader's active participation, the most significant feature of programmed learning.

The book is really a course in electrocardiography based upon principles and logical developments of them. It requires the same intense concentration as if we are listening to a highly competent lecturer. In time it will be improved, as it already has been in this text over the one originally constructed in 1963. Built into programme learning is the opportunity for research in teaching methodology. At present the learner who works through this book has one of the best, most logical and clear thinking teachers. It has already been used in an important experiment at Newcastle to compare the relative efficiency of a good teaching machine programme, with a course of very carefully prepared and well delivered lectures with identical content.

The results involving 77 fifth year medical students with little previous knowledge of the subject showed that the teaching machine produced results just as good as very carefully prepared lectures. For academically poorer students, and for those whose native tongue was not English, the programme was much the more effective teaching method. Eighty-three percent of the students considered this method to be more effective than listening to lectures or reading a conventional text-book, while 69 per cent found it easier to concentrate with this method than during lectures and 75 per cent concentrated better with it then while reading.

Even the best electrocardiographer is not necessarily aware of the basic principles and the logical order of ideas upon which his interpretations depend. The book is highly recommended to all students, physicians, and accomplished electrocardiographers. For here, the whole world is being taught by an accomplished teacher.

MEDICAL PHARMACOLOGY: Principles and Concepts. 4th Edition. Edited by Andres Goth, M.D. The C. V. Mosby Company, St. Louis, 1968, 749 pp. $13.50.

Reviewed by: LOUIS H. NAHUM

This is the 4th edition of a highly popular book on medical physiology. It is important to the physician because what he learns in medical school in a relatively short course is not sufficient to prepare him for sophisticated therapy at the bedside with drugs. It presents, in a concise manner, those principles and concepts of pharmacology that are essential for the proper utilization of the therapeutic agents available to the physician. This edition lays increased emphasis on the basic aspects of the mode of action of drugs and, in addition, has a completely rewritten chapter on general anesthetics and a wholly new chapter on contemporary drug abuse by Dr. Gregory G. Dimijian from the Department of Psychiatry.

The author recognizes that his task is to produce a concise text rather than a reference manual and has done this superbly. Current concepts about drug effects can be quite intricate, there is not enough time for mastering them in a crowded medical curriculum and busy practice and yet information about drugs and their action and how they are used in basic research must be available to each physician. In this 4th edition it is.

One will find in it the conventional 11 chapters: general aspects, drug effects on the nervous system, psychopharmacology depressant and stimulants of the central nervous system, anesthetics, drugs used in cardiovascular disease, effects of drugs on the gastrointestinal tract, drugs influencing metabolic and endocrine function, chemotherapy, poisons and antidotes, a last chapter on prescription writing and drugs and an excellent index. With this book and AMA New Drugs 1967 one can become a rational and skillful therapeutist.

SYSTEMIC MYCOSES, A Ciba Foundation Symposium edited by G. E. W. Wolstenholme and Ruth Porter. Boston, Little, Brown and Co., 1968. 287 pp with 49 illustrations. Price $12.00.

Reviewed by: HERBERT LEVINE

This volume consists of papers presented at a symposium held in Ibadan, Nigeria, March 29-31, 1967, under the auspices of the Ciba Foundation. Some of the confusion in terminology in this field is dispelled by a clarifying introductory note by the editors. There follows an interesting discussion of William Balfour Baikie, to whom the symposium was dedicated. Baikie, a Scottish physician turned explorer, led the first successful expedition into the hinterland of Nigeria in 1854. This feat was achieved because of the use of cinchona bark as a prophylaxis against malaria, which disease had decimated several previous expeditions. Baikie remained in Nigeria to set up trading posts and to write up his observations of geography, economics, and native society and culture.

Papers concerned with organ distribution of deep mycoses, pathogenesis, and histopathology follow. An article which is paticularly informative, by Seelinger of Germany, describes the application of new immunological techniques to the diagnosis of deep mycoses.

The remaining papers are devoted to clinical and radiological aspects, epidemiology, and therapy with anti-fungal agents. MacKinnon, of Uruguay, discusses the relationship of ambient temperature and humidity to the pathogenecity of several fungi, and accounts for the geographical distibution of clinical disease on this basis. All these topics are covered in a reasonably extensive fashion, and much useful information is presented. The apt use of tables and charts throughout the text contributes much to the understanding of the material.

The deep mycoses are being diagnosed with increasing frequency, and this volume represents a worthwhile summary of present knowledge of these diseases for the practicing physician.

MEDICAL NEWS

Interactions of Oral Anticoagulants With Other Drugs

Both potentiation and inhibition of anticoagulant activity have been observed in patients taking other drugs along with coumarin anticoagulants. Coumarins can also affect the activity of other drugs. Interactions have been reported less frequently with indandione anticoagulants. No method is available for predicting the occurrence or degree of interaction. Its extent may vary greatly from patient to patient, mainly because of differences in rate of metabolism; interactions have, in some cases, been serious enough to cause death.

Mechanisms of Drug Interaction—Some drugs increase microsomal enzyme activity in the vlier, thus stimulating metabolic degradition of the coumarins and reducing their anticoagulant effect; patients are then likely to need larger amounts of anticoagulant, and when the drugs are discontinued, the dose of the anticoagulant may have be reduced (S. A. Cucinell et al., Clin. Pharmacol. Ther., 6:420, 1965). The drugs most clearly implicated in reports of such interactions are phenobarbital and chloral hydrate; other drugs with a potential for microsomal enzyme stimulation include other barbiturates, glutethimide (Doriden), meprobamate, grisofulvin, and haloperidol (Haldol). Phenyramidol (Analexin) may inhibit the metabolic degradation of anticoagulants and thus increase their effect.

Potentiating effects may also occur with drugs that displace the anticoagulant from protein binding sites in plasma, thus greatly increasing the peak concentration of free coumarin P. A. Aggeler et al., New Eng. J. Med., 276:497, 1967). Drugs having this effect include phenylbutazone (Butazolidin), oxyphenbutazone (Tandearil), clofibrate (Atromid-S), diphenylhydantoin (Dilantin), and salicylates.

Sulfisoxazole Gantrisin, and other brands), chloramphenicol (Chloromycetin), tetracyclines, neomycin, and possibly other antibiotics may prolong prothrombin time in patients on oral anticoagulant drugs, mainly by interference with vitamin K production by gut bacteria. Quinine, quindine, norethandrolone (Nilevar), and dextrothyroxine (Choloxin) also increase the anticoagulant effects of coumarin, though the mechanisms are unclear.

Potentiation Effects of Coumarin on Other Drugs—Coumarins elevate serum concentrations of diphenylhydantoin, probably by inhibiting enzymatic degradation of diphenylhydantoin in the liver. Diphenylhydantoin toxicity has been reported in patients receiving both drugs J. M. Hansen et al., Lancet, 2:265, 1966; N. O. Rothermich, Lancet, 2:-640, 1966). Coumarins also potentiate the hypoglycemic effect of tolbutamide (Orinase) apparently by inhibiting its conversion to carboxytolbutamide in the liver (M. Kristensen and J. M. Hansen, Diabetes, 16:211, April, 1967).

Conclusion—Careful attention to the dosage of oral anticoagulants is required both during administration and following withdrawal of drugs which potentiate or inhibit anticoagulant effects. Preferably, the concurrent use of anticoagulants and interacting drugs should be avoided. For a recent review of "Pharmacological Implications of Microsomal Enzyme Induction" see A. H. Conney, Pharmacol. Rev., 19:317, September, 1967).

Reprinted from *The Medical Letter on Drugs and Therapeutics*, New York, N.Y., Vol. 9, No. 24, December 1, 1967

Friend of Medicine Passes

Elwood Charles Stanley, Sr., 65, of 419 White Plains Road, Trumbull, died October 31, 1968 at Bridgeport Hospital.

He was an outstanding public spirited business leader who served the citizens of Connecticut without financial remuneration, donating unselfishly of his time, talents and compassion for his fellow man.

He was appointed to the Tuberculosis Commission on August 5, 1947, and was elected chairman on July 1, 1949, serving as chairman through the successive changes of that Commission until his death.

Under his leadership, the deaths from tuberculosis in Connecticut dropped from 506 in 1947 to 67 in 1967. New cases per year were reduced from 1,200 to 591, and the five state tuberculosis hospitals were consolidated to three chronic disease hospitals.

His understanding and guidance directed and united the efforts of members of the two separate commissions as they became the Commission on Tuberculosis and Other Chronic Illness, and as this commission in turn became a part of the expanded State Department of Health in October 1959.

Mr. Stanley has also served as a most active member of the Public Health Council since 1959.

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